=> file reg; d rn cn l3; d rn cn l4
FILE 'REGISTRY' ENTERED AT 11:16:09 ON 29 OCT 2003

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 27 OCT 2003 HIGHEST RN 609766-09-8
DICTIONARY FILE UPDATES: 27 OCT 2003 HIGHEST RN 609766-09-8

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN **362516-16-3** REGISTRY
CN Kinase (phosphorylating), IκB protein, α (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Conserved helix-loop-helix ubiquitous kinase
CN IκB kinase α
CN IKKα kinase
CN IKK1 kinase
CN Protein kinase CHUK
CN Protein kinase IKKα

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN **362517-43-9** REGISTRY
CN Kinase (phosphorylating), IκB protein, β (9CI) (CA INDEX NAME)
OTHER NAMES:
CN IκB kinase β
CN IκB protein kinase β
CN IκB protein kinase 2
CN IKKβ kinase
CN IKK2 kinase

=> => file hcaplus; d que 116; d que 117; d que 119; d que 123; d que 129
FILE 'HCAPLUS' ENTERED AT 13:18:21 ON 29 OCT 2003

FILE COVERS 1907 - 29 Oct 2003 VOL 139 ISS 18
FILE LAST UPDATED: 28 Oct 2003 (20031028/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L3	1	SEA FILE=REGISTRY ABB=ON PLU=ON 362516-16-3/RN
L4	1	SEA FILE=REGISTRY ABB=ON PLU=ON 362517-43-9/RN
L5	569	SEA FILE=HCAPLUS ABB=ON PLU=ON INFLAMMATION/CT (L) ANTI
L6	48776	SEA FILE=HCAPLUS ABB=ON PLU=ON ANTI-INFLAMMATORY AGENTS+PFT/CT
L7	310	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 OR L4
L8	1222	SEA FILE=HCAPLUS ABB=ON PLU=ON IKK? OR PROTEIN KINASE (W) (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (BETA) OR IKB
L9	16455	SEA FILE=HCAPLUS ABB=ON PLU=ON NEMO OR NF (2W) ESSENTIAL MODULAT? OR NF KAPPA? OR NFKAPPA?
L10	6125	SEA FILE=HCAPLUS ABB=ON PLU=ON SELECTINS+OLD/CT
L16	2	SEA FILE=HCAPLUS ABB=ON PLU=ON (L5 OR L6) AND (L7 OR L8) AND L9 AND L10

L3	1	SEA FILE=REGISTRY ABB=ON PLU=ON 362516-16-3/RN
L4	1	SEA FILE=REGISTRY ABB=ON PLU=ON 362517-43-9/RN
L5	569	SEA FILE=HCAPLUS ABB=ON PLU=ON INFLAMMATION/CT (L) ANTI
L6	48776	SEA FILE=HCAPLUS ABB=ON PLU=ON ANTI-INFLAMMATORY AGENTS+PFT/CT
L7	310	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 OR L4
L8	1222	SEA FILE=HCAPLUS ABB=ON PLU=ON IKK? OR PROTEIN KINASE (W) (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (BETA) OR IKB
L9	16455	SEA FILE=HCAPLUS ABB=ON PLU=ON NEMO OR NF (2W) ESSENTIAL MODULAT? OR NF KAPPA? OR NFKAPPA?
L11	4119	SEA FILE=HCAPLUS ABB=ON PLU=ON OSTEOCLAST+OLD/CT
L17	3	SEA FILE=HCAPLUS ABB=ON PLU=ON (L5 OR L6) AND (L7 OR L8) AND L9 AND L11

L3	1	SEA FILE=REGISTRY ABB=ON PLU=ON 362516-16-3/RN
L4	1	SEA FILE=REGISTRY ABB=ON PLU=ON 362517-43-9/RN
L5	569	SEA FILE=HCAPLUS ABB=ON PLU=ON INFLAMMATION/CT (L) ANTI
L6	48776	SEA FILE=HCAPLUS ABB=ON PLU=ON ANTI-INFLAMMATORY AGENTS+PFT/CT
L7	310	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 OR L4
L8	1222	SEA FILE=HCAPLUS ABB=ON PLU=ON IKK? OR PROTEIN KINASE (W) (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (BETA) OR IKB
L9	16455	SEA FILE=HCAPLUS ABB=ON PLU=ON NEMO OR NF (2W) ESSENTIAL MODULAT? OR NF KAPPA? OR NFKAPPA?
L13	661	SEA FILE=HCAPLUS ABB=ON PLU=ON ANTENNAPED?
L19	2	SEA FILE=HCAPLUS ABB=ON PLU=ON (L5 OR L6) AND (L7 OR L8) AND L9 AND L13

Prepared by Toby Port 308-3534, Biotech Library

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L3          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  362516-16-3/RN
L4          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  362517-43-9/RN
L5        569 SEA FILE=HCAPLUS ABB=ON  PLU=ON  INFLAMMATION/CT (L) ANTI
L6      48776 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTI-INFLAMMATORY AGENTS+PFT/C
              T
L7        310 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 OR L4
L8       1222 SEA FILE=HCAPLUS ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
              (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (BETA) OR IKB
L9      16455 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
              MODULAT? OR NF KAPPA? OR NFKAPPA?
L21     97170 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SIGNAL TRANSDUCTION, BIOLOGICA
              L+PFT/CT
L22        24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L5 OR L6) AND (L7 OR L8) AND
              L9 AND L21
L23         8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 AND (RAS OR IKK4 OR TRAF6
              OR BMS OR TGF OR VASCULAR ENDO? OR A20 OR PYRIN)/TI


L3          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  362516-16-3/RN
L4          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  362517-43-9/RN
L5        569 SEA FILE=HCAPLUS ABB=ON  PLU=ON  INFLAMMATION/CT (L) ANTI
L6      48776 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTI-INFLAMMATORY AGENTS+PFT/C
              T
L7        310 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 OR L4
L8       1222 SEA FILE=HCAPLUS ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
              (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (BETA) OR IKB
L24     10064 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NUCLEAR FACTOR KAPPA B
L26        22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L5 OR L6) AND (L7 OR L8) AND
              L24 (5A) INHIBIT?
L28     962409 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PROTEINS/CW OR PROTEIN/CW
L29          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 AND L28

=> s l16 or l17 or l19 or l23 or l29
L114        11 L16 OR L17 OR L19 OR L23 OR L29

=> file medline; d que l43; d que l44; d que l46; d que l47; d que l54; d que l56
FILE 'MEDLINE' ENTERED AT 13:19:15 ON 29 OCT 2003

 FILE LAST UPDATED: 28 OCT 2003 (20031028/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L30     86407 SEA FILE=MEDLINE ABB=ON  PLU=ON  INFLAMMATION+NT/CT
L31    257645 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTI-INFLAMMATORY AGENTS+NT/CT

L32       687 SEA FILE=MEDLINE ABB=ON  PLU=ON  I KAPPA B KINASE/CN
L33      8292 SEA FILE=MEDLINE ABB=ON  PLU=ON  NEMO OR NF-KAPPAB OR NBD
              PEPTIDE, MOUSE/CN
```

L34	6737	SEA FILE=MEDLINE ABB=ON	PLU=ON	SELECTINS+NT/CT
L43	2	SEA FILE=MEDLINE ABB=ON AND L34	PLU=ON	(L30 OR L31) AND L32 AND L33
L30	86407	SEA FILE=MEDLINE ABB=ON	PLU=ON	INFLAMMATION+NT/CT
L31	257645	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANTI-INFLAMMATORY AGENTS+NT/CT
L32	687	SEA FILE=MEDLINE ABB=ON	PLU=ON	I KAPPA B KINASE/CN
L33	8292	SEA FILE=MEDLINE ABB=ON PEPTIDE, MOUSE/CN	PLU=ON	NEMO OR NF-KAPPAB OR NBD
L35	5541	SEA FILE=MEDLINE ABB=ON	PLU=ON	OSTEOCLASTS+NT/CT
L44	0	SEA FILE=MEDLINE ABB=ON AND L35	PLU=ON	(L30 OR L31) AND L32 AND L33
L30	86407	SEA FILE=MEDLINE ABB=ON	PLU=ON	INFLAMMATION+NT/CT
L31	257645	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANTI-INFLAMMATORY AGENTS+NT/CT
L32	687	SEA FILE=MEDLINE ABB=ON	PLU=ON	I KAPPA B KINASE/CN
L33	8292	SEA FILE=MEDLINE ABB=ON PEPTIDE, MOUSE/CN	PLU=ON	NEMO OR NF-KAPPAB OR NBD
L37	197	SEA FILE=MEDLINE ABB=ON PROTEIN/CN	PLU=ON	ANTENNAPEDIA HOMEODOMAIN
L46	0	SEA FILE=MEDLINE ABB=ON AND L37	PLU=ON	(L30 OR L31) AND L32 AND L33
L30	86407	SEA FILE=MEDLINE ABB=ON	PLU=ON	INFLAMMATION+NT/CT
L31	257645	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANTI-INFLAMMATORY AGENTS+NT/CT
L32	687	SEA FILE=MEDLINE ABB=ON	PLU=ON	I KAPPA B KINASE/CN
L33	8292	SEA FILE=MEDLINE ABB=ON PEPTIDE, MOUSE/CN	PLU=ON	NEMO OR NF-KAPPAB OR NBD
L38	4	SEA FILE=MEDLINE ABB=ON	PLU=ON	"TAT PEPTIDE (37-72)"/CN
L39	5	SEA FILE=MEDLINE ABB=ON	PLU=ON	"HIV-1 TAT PROTEIN (48-60)"/CN
L40	792	SEA FILE=MEDLINE ABB=ON	PLU=ON	HIV-1 TAT
L47	0	SEA FILE=MEDLINE ABB=ON AND (L38 OR L39 OR L40)	PLU=ON	(L30 OR L31) AND L32 AND L33
L30	86407	SEA FILE=MEDLINE ABB=ON	PLU=ON	INFLAMMATION+NT/CT
L31	257645	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANTI-INFLAMMATORY AGENTS+NT/CT
L32	687	SEA FILE=MEDLINE ABB=ON	PLU=ON	I KAPPA B KINASE/CN
L49	11019	SEA FILE=MEDLINE ABB=ON	PLU=ON	NF-KAPPA B/CT
L51	15438	SEA FILE=MEDLINE ABB=ON	PLU=ON	DOWN-REGULATION/CT
L53	5	SEA FILE=MEDLINE ABB=ON AND L51	PLU=ON	(L30 OR L31) AND L32 AND L49
L54	1	SEA FILE=MEDLINE ABB=ON	PLU=ON	L53 AND VEGF/TI
L30	86407	SEA FILE=MEDLINE ABB=ON	PLU=ON	INFLAMMATION+NT/CT
L31	257645	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANTI-INFLAMMATORY AGENTS+NT/CT

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L32          687 SEA FILE=MEDLINE ABB=ON  PLU=ON  I KAPPA B KINASE/CN
L50         1741 SEA FILE=MEDLINE ABB=ON  PLU=ON  NF-KAPPA B/CT (L) AI/CT
L55           31 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L30 OR L31) AND L32 AND L50
L56            6 SEA FILE=MEDLINE ABB=ON  PLU=ON  L55 AND (NEMO OR IKK OR
                  ENDOTHELIAL OR POTENTIAL OR PIVOTAL)/TI


=> s l43 or l54 or l56
L115           9 L43 OR L54 OR L56

=> file embase; d que l68; d que l69; d que l71; d que l77
FILE 'EMBASE' ENTERED AT 13:19:59 ON 29 OCT 2003
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 FILE COVERS 1974 TO 23 Oct 2003 (20031023/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L57       713484 SEA FILE=EMBASE ABB=ON  PLU=ON  INFLAMMATION+NT/CT
L58        13290 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIINFLAMMATORY AGENT/CT
L59         4088 SEA FILE=EMBASE ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                  (CHUK OR IKK?) OR (IK OR I KAPPA) OR I KAPPA (W) (B OR BETA)
L60        11421 SEA FILE=EMBASE ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                  MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE, MOUSE
L61         1205 SEA FILE=EMBASE ABB=ON  PLU=ON  SELECTIN+NT/CT
L68            0 SEA FILE=EMBASE ABB=ON  PLU=ON  (L57 OR L58) AND L59 AND L60
                  AND L61


L57       713484 SEA FILE=EMBASE ABB=ON  PLU=ON  INFLAMMATION+NT/CT
L58        13290 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIINFLAMMATORY AGENT/CT
L59         4088 SEA FILE=EMBASE ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                  (CHUK OR IKK?) OR (IK OR I KAPPA) OR I KAPPA (W) (B OR BETA)
L60        11421 SEA FILE=EMBASE ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                  MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE, MOUSE
L62         5890 SEA FILE=EMBASE ABB=ON  PLU=ON  OSTEOCLAST+NT/CT
L69            4 SEA FILE=EMBASE ABB=ON  PLU=ON  (L57 OR L58) AND L59 AND L60
                  AND L62


L57       713484 SEA FILE=EMBASE ABB=ON  PLU=ON  INFLAMMATION+NT/CT
L58        13290 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIINFLAMMATORY AGENT/CT
L59         4088 SEA FILE=EMBASE ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                  (CHUK OR IKK?) OR (IK OR I KAPPA) OR I KAPPA (W) (B OR BETA)
L60        11421 SEA FILE=EMBASE ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                  MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE, MOUSE
L64          437 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTENNAPEDIA
L71            0 SEA FILE=EMBASE ABB=ON  PLU=ON  (L57 OR L58) AND L59 AND L60
                  AND L64


L57       713484 SEA FILE=EMBASE ABB=ON  PLU=ON  INFLAMMATION+NT/CT
L58        13290 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIINFLAMMATORY AGENT/CT
L59         4088 SEA FILE=EMBASE ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                  (CHUK OR IKK?) OR (IK OR I KAPPA) OR I KAPPA (W) (B OR BETA)
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L60        11421 SEA FILE=EMBASE ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                 MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE, MOUSE
L65        98144 SEA FILE=EMBASE ABB=ON  PLU=ON  SIGNAL TRANSDUCTION/CT
L73        41485 SEA FILE=EMBASE ABB=ON  PLU=ON  GENE EXPRESSION REGULATION+NT/C
                 T
L76           14 SEA FILE=EMBASE ABB=ON  PLU=ON  (L57 OR L58) AND L59 AND L60
                 AND L65 AND L73
L77            2 SEA FILE=EMBASE ABB=ON  PLU=ON  L76 AND (PHORBOL OR MUCOSAL)/TI


=> s l69 or l77
L116           6 L69 OR L77

=> file biosis; d que l91; d que l93; d que l94; d que l95; d que l100
FILE 'BIOSIS' ENTERED AT 13:21:55 ON 29 OCT 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 22 October 2003 (20031022/ED)

FILE RELOADED: 19 October 2003.


L78       267784 SEA FILE=BIOSIS ABB=ON  PLU=ON  INFLAMMAT? OR ANTI INFLAMM? OR
                 ANTIINFLAMM?
L79         3163 SEA FILE=BIOSIS ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                 (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (B OR BETA)
L80        16659 SEA FILE=BIOSIS ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                 MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE
L81        10764 SEA FILE=BIOSIS ABB=ON  PLU=ON  SELECTIN
L90           16 SEA FILE=BIOSIS ABB=ON  PLU=ON  L78 AND L79 AND L80 AND L81
L91            3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L90 AND (SELECTIVE OR INDUCIBLE
                  OR BOVINE)/TI


L78       267784 SEA FILE=BIOSIS ABB=ON  PLU=ON  INFLAMMAT? OR ANTI INFLAMM? OR
                 ANTIINFLAMM?
L79         3163 SEA FILE=BIOSIS ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                 (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (B OR BETA)
L80        16659 SEA FILE=BIOSIS ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                 MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE
L82         9736 SEA FILE=BIOSIS ABB=ON  PLU=ON  OSTEOCLAST
L92            2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L78 AND L79 AND L80 AND L82
L93            1 SEA FILE=BIOSIS ABB=ON  PLU=ON  L92 AND IKAPPAB/TI


L78       267784 SEA FILE=BIOSIS ABB=ON  PLU=ON  INFLAMMAT? OR ANTI INFLAMM? OR
                 ANTIINFLAMM?
L79         3163 SEA FILE=BIOSIS ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                 (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (B OR BETA)
L80        16659 SEA FILE=BIOSIS ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                 MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE
L84          668 SEA FILE=BIOSIS ABB=ON  PLU=ON  ANTENNAPEDIA
L94            0 SEA FILE=BIOSIS ABB=ON  PLU=ON  L78 AND L79 AND L80 AND L84
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L78      267784 SEA FILE=BIOSIS ABB=ON  PLU=ON  INFLAMMAT? OR ANTI INFLAMM? OR
                ANTIINFLAMM?
L79        3163 SEA FILE=BIOSIS ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (B OR BETA)
L80       16659 SEA FILE=BIOSIS ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE
L85        1035 SEA FILE=BIOSIS ABB=ON  PLU=ON  HIV-1 TAT
L95           0 SEA FILE=BIOSIS ABB=ON  PLU=ON  L78 AND L79 AND L80 AND L85


L78      267784 SEA FILE=BIOSIS ABB=ON  PLU=ON  INFLAMMAT? OR ANTI INFLAMM? OR
                ANTIINFLAMM?
L79        3163 SEA FILE=BIOSIS ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (B OR BETA)
L80       16659 SEA FILE=BIOSIS ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE
L83       56032 SEA FILE=BIOSIS ABB=ON  PLU=ON  TRANSCRIPTION FACTOR
L87       20306 SEA FILE=BIOSIS ABB=ON  PLU=ON  DOWN REGULATION
L88       18656 SEA FILE=BIOSIS ABB=ON  PLU=ON  GENE EXPRESSION (2A) REGULAT?
L98          22 SEA FILE=BIOSIS ABB=ON  PLU=ON  L78 AND L79 AND L80 AND L83
                AND (L87 OR L88)
L100          3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L98 AND (SUBUNITS OR PLATELETS
                OR CYTOKINE)/TI NOT (POLAPREZINC OR RANTES)/TI


=> s l19 or l93 or l100
'ANTI-INFLAMMATORY AGENTS' NOT IN RELATIONSHIP FILE
RELATIONSHIP CODE 'PFT' IGNORED
         2554 INFLAMMATION/CT
       454995 ANTI
           14 ANTIS
       455004 ANTI
                (ANTI OR ANTIS)
            3 INFLAMMATION/CT (L) ANTI
          113 ANTI-INFLAMMATORY AGENTS+PFT/CT  (1 TERM)
           12 L3
            5 L4
          881 IKK?
      1334996 PROTEIN
       506192 PROTEINS
      1538553 PROTEIN
                (PROTEIN OR PROTEINS)
       244924 KINASE
        36360 KINASES
       253214 KINASE
                (KINASE OR KINASES)
       117386 PROTEIN KINASE
                (PROTEIN(W)KINASE)
           14 CHUK
          881 IKK?
            1 PROTEIN KINASE (W) (CHUK OR IKK?)
         1859 IK
          433 IKS
         2212 IK
                (IK OR IKS)
       830202 I
        38641 KAPPA
          105 KAPPAS
```

```
 38693 KAPPA
         (KAPPA OR KAPPAS)
  2830 I KAPPA
         (I(W)KAPPA)
612625 BETA
   437 BETAS
612715 BETA
         (BETA OR BETAS)
    18 (IK OR I KAPPA) (W) (BETA)
   255 IKB
     4 IKBS
   257 IKB
         (IKB OR IKBS)
   165 NEMO
 23184 NF
   696 NFS
 23662 NF
         (NF OR NFS)
171074 ESSENTIAL
   480 ESSENTIALS
171498 ESSENTIAL
         (ESSENTIAL OR ESSENTIALS)
217279 MODULAT?
    68 ESSENTIAL MODULAT?
         (ESSENTIAL(W)MODULAT?)
    31 NF (2W) ESSENTIAL MODULAT?
 23184 NF
   696 NFS
 23662 NF
         (NF OR NFS)
 41362 KAPPA?
 15785 NF KAPPA?
         (NF(W)KAPPA?)
  1670 NFKAPPA?
   668 ANTENNAPED?
L117       4 L19 OR L93 OR L100

=> file wpid; d que l112
FILE 'WPIDS' ENTERED AT 13:22:34 ON 29 OCT 2003
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FILE LAST UPDATED:          27 OCT 2003      <20031027/UP>
MOST RECENT DERWENT UPDATE:     200369        <200369/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE


>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
    http://thomsonderwent.com/coverage/latestupdates/           <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://thomsonderwent.com/support/userguides/               <<<


                    Prepared by Toby Port  308-3534, Biotech Library
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L101       58745 SEA FILE=WPIDS ABB=ON  PLU=ON  INFLAMMAT? OR ANTI INFLAMM? OR
                 ANTIINFLAMM?
L102         115 SEA FILE=WPIDS ABB=ON  PLU=ON  IKK? OR PROTEIN KINASE (W)
                 (CHUK OR IKK?) OR (IK OR I KAPPA) (W) (B OR BETA)
L103         402 SEA FILE=WPIDS ABB=ON  PLU=ON  NEMO OR NF (2W) ESSENTIAL
                 MODULAT? OR NF KAPPA? OR NFKAPPA? OR NBD PEPTIDE
L111          18 SEA FILE=WPIDS ABB=ON  PLU=ON  L101 AND L102 AND L103
L112          15 SEA FILE=WPIDS ABB=ON  PLU=ON  L111 AND (AMINOPYR? OR NEMO OR
                 KAPPAB OR KAPPA B OR NFKAPPAB)/TI


=> dup rem l115 l114 l116 l117 l112
FILE 'MEDLINE' ENTERED AT 13:23:09 ON 29 OCT 2003

FILE 'HCAPLUS' ENTERED AT 13:23:09 ON 29 OCT 2003
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PROCESSING COMPLETED FOR L115
PROCESSING COMPLETED FOR L114
PROCESSING COMPLETED FOR L116
PROCESSING COMPLETED FOR L117
PROCESSING COMPLETED FOR L112
L118          41 DUP REM L115 L114 L116 L117 L112 (4 DUPLICATES REMOVED)
                 ANSWERS '1-9' FROM FILE MEDLINE
                 ANSWERS '10-20' FROM FILE HCAPLUS
                 ANSWERS '21-26' FROM FILE EMBASE
                 ANSWERS '27-29' FROM FILE BIOSIS
                 ANSWERS '30-41' FROM FILE WPIDS

=> d ibib ab l118 1-41

L118 ANSWER 1 OF 41     MEDLINE on STN
ACCESSION NUMBER:    2003448102     MEDLINE
DOCUMENT NUMBER:     22840665   PubMed ID: 12763940
TITLE:               Inhibition of NF-kappaB by a TAT-NEMO-binding
                     domain peptide accelerates constitutive apoptosis and
                     abrogates LPS-delayed neutrophil apoptosis.
AUTHOR:              Choi Mira; Rolle Susanne; Wellner Maren; Cardoso M
                     Cristina; Scheidereit Claus; Luft Friedrich C; Kettritz
                     Ralph
CORPORATE SOURCE:    Division of Nephrology, Franz Volhard Clinic, Medical
                     Faculty of the Charite, Humboldt Univertsity of Berlin,
                     Wiltbergstrasse 50, 13122 Berlin, Germany.
SOURCE:              BLOOD, (2003 Sep 15) 102 (6) 2259-67.
                     Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         200310
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ENTRY DATE: Entered STN: 20030928
Last Updated on STN: 20031018
Entered Medline: 20031017

AB Delivery of biologically active peptides into human polymorphonuclear neutrophils (PMNs) has implications for studying cellular functions and may be therapeutically relevant. The transcription factor nuclear factor-kappaB (NF-kappaB) regulates the expression of multiple genes controlling inflammation, proliferation, and cell survival. PMNs play a crucial role in first-line defense. Targeting NF-kappaB in these cells may promote apoptosis and therefore facilitate resolution of inflammation. We used an 11-amino acid sequence NEMO-binding domain (NBD) that selectively inhibits the IKKgamma (NEMO)/IKKbeta interaction, preventing NF-kappaB activation. An HIV-TAT sequence served as a highly effective transducing shuttle. We show that lipopolysaccharide (LPS), granulocyte-macrophage colony-stimulating factor (GM-CSF), and dexamethasone (DEX) significantly reduced apoptosis after 20 hours. LPS, but not GM-CSF or DEX, activated NF-kappaB as shown by IkappaBalpha degradation, NF-kappaB DNA binding, and transcriptional activity. The TAT-NBD blocked LPS-induced NF-kappaB activation and NF-kappaB-dependent gene expression. TAT-NBD accelerated constitutive PMN apoptosis dose dependently and abrogated LPS-delayed apoptosis. These results provide a proof of principle for peptide delivery by TAT-derived protein transduction domains to specifically inhibit NF-kappaB activity in PMNs. This strategy may help in controlling various cellular functions even in short-lived, transfection-resistant primary human cells.

L118 ANSWER 2 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2003031264 MEDLINE
DOCUMENT NUMBER: 22426348 PubMed ID: 12538767
TITLE: **VEGF** expression in human macrophages is NF-kappaB-dependent: studies using adenoviruses expressing the endogenous NF-kappaB inhibitor IkappaBalpha and a kinase-defective form of the IkappaB kinase 2.
AUTHOR: Kiriakidis Serafim; Andreakos Evangelos; Monaco Claudia; Foxwell Brian; Feldmann Marc; Paleolog Ewa
CORPORATE SOURCE: Kennedy Institute of Rheumatology Division, Faculty of Medicine, Imperial College of Science, Technology and Medicine, London W6 8LH, UK.. s.kiriakidis@ic.ac.uk
SOURCE: JOURNAL OF CELL SCIENCE, (2003 Feb 15) 116 (Pt 4) 665-74. Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 20030123
Last Updated on STN: 20030910
Entered Medline: 20030909

AB Vascular endothelial growth factor (VEGF) is the most endothelial cell-specific angiogenic factor characterised to date, and it is produced by a variety of cell types. In macrophages, VEGF has been shown to be upregulated by the inflammatory mediator lipopolysaccharide (LPS) and by engagement of CD40 by CD40 ligand (CD40L). Because LPS and CD40L activate nuclear factor-kappaB (NF-kappaB) in monocytes, we investigated in this study whether VEGF production in macrophages, when stimulated with either LPS or CD40L, is NF-kappaB-dependent. We used adenoviral constructs over-expressing either IkappaBalpha (AdvIkappaBalpha), the endogenous inhibitor of NF-kappaB, or a kinase-defective mutant of IKK-2 (AdvIKK-2dn), an upstream activator of IkappaBalpha, to infect normal human monocyte-derived macrophages. We observed that LPS-induced production of VEGF in human macrophages was almost completely inhibited

(>90%) following adenoviral transfer of IkappaBalpha. In addition, we observed significant inhibition of the CD40L-induced VEGF production in macrophages following infection with AdvIkappaBalpha. Expression of IKK-2dn in macrophages decreased VEGF production in response to LPS or CD40L by approximately 50%, suggesting that in addition to IKK-2, other kinases might be involved in NF-kappaB activation. These results show for the first time that VEGF production in human macrophages is NF-kappaB dependent. NF-kappaB regulates many of the genes involved in immune and inflammatory responses, and our study adds the angiogenic cytokine VEGF to the list of NF-kappaB-dependent cytokines.

L118 ANSWER 3 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2003279407 MEDLINE
DOCUMENT NUMBER: 22610411 PubMed ID: 12692538
TITLE: The two faces of **IKK** and NF-kappaB inhibition: prevention of systemic inflammation but increased local injury following intestinal ischemia-reperfusion.
AUTHOR: Chen Lee-Wei; Egan Laurence; Li Zhi-Wei; Greten Florian R; Kagnoff Martin F; Karin Michael
CORPORATE SOURCE: Laboratory of Gene Regulation and Signal Transduction, Department of Pharmacology, University of California, San Diego, California, USA.
SOURCE: NATURE MEDICINE, (2003 May) 9 (5) 575-81.
Journal code: 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030617
Last Updated on STN: 20030627
Entered Medline: 20030626

AB We studied the role of NF-kappaB in acute inflammation caused by gut ischemia-reperfusion through selective ablation of IkappaB kinase (IKK)-beta, the catalytic subunit of IKK that is essential for NF-kappaB activation. Ablation of IKK-beta in enterocytes prevented the systemic inflammatory response, which culminates in multiple organ dysfunction syndrome (MODS) that is normally triggered by gut ischemia-reperfusion. IKK-beta removal from enterocytes, however, also resulted in severe apoptotic damage to the reperfused intestinal mucosa. These results show the dual function of the NF-kappaB system, which is responsible for both tissue protection and systemic inflammation, and underscore the caution that should be exerted in using NF-kappaB and IKK inhibitors.

L118 ANSWER 4 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2002695383 MEDLINE
DOCUMENT NUMBER: 22323209 PubMed ID: 12221085
TITLE: IKKalpha, IKKbeta, and **NEMO**/IKKgamma are each required for the NF-kappa B-mediated inflammatory response program.
AUTHOR: Li Xiang; Massa Paul E; Hanidu Adedayo; Peet Gregory W; Aro Patrick; Savitt Ann; Mische Sheenah; Li Jun; Marcu Kenneth B
CORPORATE SOURCE: Department of Biology, Boehringer Ingelheim Pharmaceuticals, Ridgefield, Connecticut 06877-0368, USA.
CONTRACT NUMBER: GM26939 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Nov 22) 277 (47) 45129-40.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030108
Entered Medline: 20030107

AB The IKKbeta and NEMO/IKKgamma subunits of the NF-kappaB-activating signalsome complex are known to be essential for activating NF-kappaB by inflammatory and other stress-like stimuli. However, the IKKalpha subunit is believed to be dispensable for the latter responses and instead functions as an in vivo mediator of other novel NF-kappaB-dependent and -independent functions. In contrast to this generally accepted view of IKKalpha's physiological functions, we demonstrate in mouse embryonic fibroblasts (MEFs) that, akin to IKKbeta and NEMO/IKKgamma, IKKalpha is also a global regulator of tumor necrosis factor alpha- and IL-1-responsive IKK signalsome-dependent target genes including many known NF-kappaB targets such as serum amyloid A3, C3, interleukin (IL)-6, IL-11, IL-1 receptor antagonist, vascular endothelial growth factor, Ptx3, beta(2)-microglobulin, IL-1alpha, Mcp-1 and -3, RANTES (regulated on activation normal T cell expressed and secreted), Fas antigen, Jun-B, c-Fos, macrophage colony-stimulating factor, and granulocyte-macrophage colony-stimulating factor. Only a small number of NF-kappaB-dependent target genes were preferentially dependent on IKKalpha or IKKbeta. Constitutive expression of a trans-dominant IkappaBalpha superrepressor (IkappaBalphaSR) in wild type MEFs confirmed that these signalsome-dependent target genes were also dependent on NF-kappaB. A subset of NF-kappaB target genes were IKK-dependent in the absence of exogenous stimuli, suggesting that the signalsome was also required to regulate basal levels of activated NF-kappaB in established MEFs. Overall, a sizable number of novel NF-kappaB/IKK-dependent genes were identified including Secreted Frizzled, cadherin 13, protocadherin 7, CCAAT/enhancer-binding protein-beta and -delta, osteoprotegerin, FOXC2 and FOXF2, BMP-2, p75 neurotrophin receptor, caspase-11, guanylate-binding proteins 1 and 2, ApoJ/clusterin, interferon (alpha and beta) receptor 2, decorin, osteoglycin, epiregulin, proliferins 2 and 3, stromal cell-derived factor, and cathepsins B, F, and Z. SOCS-3, a negative effector of STAT3 signaling, was found to be an NF-kappaB/IKK-induced gene, suggesting that IKK-mediated NF-kappaB activation can coordinately illicit negative effects on STAT signaling.

L118 ANSWER 5 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2001436555 MEDLINE
DOCUMENT NUMBER: 21359355 PubMed ID: 11337506
TITLE: Activation of NF-kappa B via the Ikappa B kinase complex is both essential and sufficient for proinflammatory gene expression in primary endothelial cells.
AUTHOR: Denk A; Goebeler M; Schmid S; Berberich I; Ritz O; Lindemann D; Ludwig S; Wirth T
CORPORATE SOURCE: Department of Physiological Chemistry, Ulm University, Albert-Einstein-Allee 11, 89081 Ulm, Germany.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Jul 27) 276 (30) 28451-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20030105
Entered Medline: 20010823

AB Activation of the transcription factor **NF-kappaB** is necessary for full expression of tumor necrosis factor alpha (TNF-alpha)-inducible endothelial chemokines and adhesion molecules. However, a detailed analysis regarding contribution of the different **NF-kappaB** upstream components to endothelial activation has not been performed yet. We employed a retroviral infection approach to stably express transdominant (TD) mutants of IkappaBalpha, IkappaBbeta, or IkappaBepsilon and dominant negative (dn) versions of IkappaB kinases (IKK) 1 or 2 as well as a constitutively active version of IKK2 in human endothelial cells. TD IkappaBalpha, IkappaBbeta, and IkappaBepsilon were not degraded upon TNF-alpha exposure, and each prevented **NF-kappaB** activation. These TD IkappaB mutants almost completely inhibited the induction of monocyte chemoattractant protein-1, interleukin-8, intercellular adhesion molecule-1, vascular cell adhesion molecule-1, and E-selectin expression by TNF-alpha, whereas interferon-gamma-mediated up-regulation of intercellular adhesion molecule-1 and HLA-DR was not affected. Expression of dn IKK2 completely blocked TNF-alpha-induced up-regulation, whereas dn IKK1 showed a partial inhibition of expression of these molecules. Importantly, expression of constitutively active IKK2 was sufficient to drive full expression of all chemokines and adhesion molecules in the absence of cytokine. We conclude that the IKK/IkappaB/**NF-kappaB** pathway is crucial and sufficient for proinflammatory activation of endothelium.

L118 ANSWER 6 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2001227315 MEDLINE
DOCUMENT NUMBER: 21134503 PubMed ID: 11238099
TITLE: Adenovirus-mediated expression of a mutant IkappaB kinase 2 inhibits the response of **endothelial** cells to inflammatory stimuli.
AUTHOR: Oitzinger W; Hofer-Warbinek R; Schmid J A; Koshelnick Y; Binder B R; de Martin R
CORPORATE SOURCE: Department of Vascular Biology and Thrombosis Research, University of Vienna, Vienna, Austria.
SOURCE: BLOOD, (2001 Mar 15) 97 (6) 1611-7.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010502
Last Updated on STN: 20020420
Entered Medline: 20010426

AB In a variety of cell types, the transcription factor nuclear factor kappaB (NF-kappaB) functions as a mediator of stress and immune responses. In endothelial cells (ECs), it controls the expression of genes encoding, eg, cytokines, cell adhesion molecules, and procoagulatory proteins. This study investigates the effect of NF-kappaB suppression on several pathophysiologic functions of ECs, including inflammation, coagulation, and angiogenesis. A recombinant adenovirus was generated for expression of a dominant negative (dn) mutant of IkappaB kinase 2 (IKK2), a kinase that acts as an upstream activator of NF-kappaB. dnIKK2 inhibited NF-kappaB, resulting in strongly reduced nuclear translocation and DNA binding activity of the transcription factor and lack of expression of several proinflammatory markers, including E-selectin, intercellular adhesion molecule 1, vascular cell adhesion molecule 1, and interleukin-8. Concomitantly, inhibition of leukocyte binding to dnIKK2-expressing ECs could be demonstrated in a cell adhesion assay. Furthermore, expression of tissue factor as well as the ability to form capillary tubes in a matrigel assay was impaired in dnIKK2-expressing ECs. These data

demonstrate that NF-kappaB is of central importance not only for the inflammatory response but also for a number of other EC functions. Therefore, this transcription factor as well as its upstream regulatory signaling molecules may represent favorable targets for therapeutic interference.

L118 ANSWER 7 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2001140768 MEDLINE
DOCUMENT NUMBER: 21102361 PubMed ID: 11160126
TITLE: Therapeutic **potential** of inhibition of the NF-kappaB pathway in the treatment of inflammation and cancer.
AUTHOR: Yamamoto Y; Gaynor R B
CORPORATE SOURCE: Division of Hematology-Oncology, Department of Medicine, Harold Simmons Cancer Center, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, Texas 75390-8594, USA.
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (2001 Jan) 107 (2) 135-42. Ref: 47
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20020420
Entered Medline: 20010308

L118 ANSWER 8 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2000431571 MEDLINE
DOCUMENT NUMBER: 20425271 PubMed ID: 10968790
TITLE: Selective inhibition of **NF-kappaB** activation by a peptide that blocks the interaction of **NEMO** with the IkappaB kinase complex.
AUTHOR: May M J; D'Acquisto F; Madge L A; Glockner J; Pober J S; Ghosh S
CORPORATE SOURCE: Section of Immunobiology and Department of Molecular Biophysics and Biochemistry, Howard Hughes Medical Institute, Yale University School of Medicine, New Haven, CT 06510, USA.
CONTRACT NUMBER: AI 33443 (NIAID)
SOURCE: SCIENCE, (2000 Sep 1) 289 (5484) 1550-4.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20020420
Entered Medline: 20000914
AB Activation of the transcription factor nuclear factor (**NF**)-**kappaB** by proinflammatory stimuli leads to increased expression of genes involved in inflammation. Activation of **NF-kappaB** requires the activity of an inhibitor of kappaB (IkappaB)-kinase (IKK) complex containing two kinases (IKKalpha and IKKbeta) and the regulatory protein **NEMO** (**NF-kappaB** essential modifier). An amino-terminal alpha-helical region of **NEMO** associated with a

carboxyl-terminal segment of IKKalpha and IKKbeta that we term the **NEMO**-binding domain (NBD). A cell-permeable NBD peptide blocked association of **NEMO** with the IKK complex and inhibited cytokine-induced **NF-kappaB** activation and **NF-kappaB**-dependent gene expression. The peptide also ameliorated inflammatory responses in two experimental mouse models of acute inflammation. The NBD provides a target for the development of drugs that would block proinflammatory activation of the IKK complex without inhibiting basal **NF-kappaB** activity.

L118 ANSWER 9 OF 41 MEDLINE on STN
ACCESSION NUMBER: 1999092801 MEDLINE
DOCUMENT NUMBER: 99092801 PubMed ID: 9876974
TITLE: Nuclear factor kappa B: a **pivotal** role in the systemic inflammatory response syndrome and new target for therapy.
COMMENT: Comment in: Intensive Care Med. 1998 Nov;24(11):1129-30
AUTHOR: Christman J W; Lancaster L H; Blackwell T S
CORPORATE SOURCE: Department of Medicine, Vanderbilt University School of Medicine and the Department of Veterans Affairs, Nashville, TN 37322-2650, USA.. john.christman@mcmail.vanderbilt.edu
CONTRACT NUMBER: HL 07123 (NHLBI)
SOURCE: INTENSIVE CARE MEDICINE, (1998 Nov) 24 (11) 1131-8. Ref: 81
Journal code: 7704851. ISSN: 0342-4642.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 20020420
Entered Medline: 19990305

AB NF-kappaB is an important transcription factor complex that appears to play a fundamental role in regulating acute inflammation through activation of the cytokine cascade and production of other pro-inflammatory mediators. There is increasing evidence that NF-kappaB is important in the pathobiology of disease states such as SIRS, MODS and ARDS; therefore, therapeutic interventions aimed at limiting NF-kappaB activation and down-regulating production of inflammatory mediators could prove to be beneficial in decreasing host-derived tissue injury and organ dysfunction. Specific interventions that hold promise for suppressing NF-kappaB activation include the use of antioxidants, inhibition of NIK and the IKK signalsome, treatment with proteasome inhibitors, induction of endotoxin tolerance and, possibly the use of corticosteroids in selected patients.

L118 ANSWER 10 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:814829 HCAPLUS
DOCUMENT NUMBER: 137:320304
TITLE: Anti-inflammatory compounds and uses thereof
INVENTOR(S): May, Michael J.; Ghosh, Sankar
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 643,260.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002156000	A1	20021024	US 2001-847940	20010502
US 2003054999	A1	20030320	US 2001-847946	20010502

PRIORITY APPLN. INFO.: US 2000-201261P P 20000502
US 2000-643260 A2 20000822

AB The present invention provides anti-inflammatory compds., pharmaceutical compns. thereof, and methods of use thereof for treating inflammatory disorders. The present invention also provides methods of identifying anti-inflammatory compds. and methods of inhibiting **NF**-. **kappa**.B-dependent target gene expression in a cell. A cell-permeable peptide encompassing **NEMO** binding domain of IκB kinase was able to not only inhibit TNFα-induced **NF**-κ B activation but also reduce expression of E-selectin, an **NF**-κ B-dependent target gene, in primary human endothelial cells.

L118 ANSWER 11 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2001:816734 HCAPLUS
DOCUMENT NUMBER: 135:352790
TITLE: Anti-inflammatory compounds and uses thereof
INVENTOR(S): May, Michael J.; Ghosh, Sankar; Findeis, Mark A.; Phillips, Kathryn
PATENT ASSIGNEE(S): Praecis Pharmaceuticals Incorporated, USA; Yale University
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083554	A2	20011108	WO 2001-US14346	20010502
WO 2001083554	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1280820	A2	20030205	EP 2001-935035	20010502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003054999	A1	20030320	US 2001-847946	20010502

PRIORITY APPLN. INFO.: US 2000-201261P P 20000502
US 2000-643260 A 20000822
WO 2001-US14346 W 20010502

OTHER SOURCE(S): MARPAT 135:352790

AB The present invention provides anti-inflammatory compds., pharmaceutical compns. thereof, and methods of use thereof for treating inflammatory disorders. The present invention also provides methods of identifying anti-inflammatory compds. and methods of inhibiting **NF**-. **kappa**.B-dependent target gene expression in a cell. The present invention is based , at least in part, on the identification of the

NEMO (**NF**-κ B **essential modulator**) binding domain (NBD) on IκB kinase-α (**IKK**.alpha.) and on IκB kinase-β (**IKK**.beta.). Accordingly, in one aspect, the present invention provides anti-inflammatory compds. which are peptides comprising a **NEMO** binding domain. In on embodiment, the present invention provides anti-inflammatory compds. comprising fusion peptides of a **NEMO** binding domain and at least one membrane translocation domain. The membrane translocation domain facilitates membrane translocation of the anti-inflammatory compds.

L118 ANSWER 12 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2001:816727 HCAPLUS
DOCUMENT NUMBER: 135:352789
TITLE: Anti-inflammatory compounds inhibiting **NF-.kappa.**B-dependent target gene expression in a cell
INVENTOR(S): May, Michael J.; Ghosh, Sankar
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083547	A2	20011108	WO 2001-US40654	20010502
WO 2001083547	A3	20020516		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1282643	A2	20030212	EP 2001-931171	20010502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003054999	A1	20030320	US 2001-847946	20010502

PRIORITY APPLN. INFO.: US 2000-201261P P 20000502
US 2000-643260 A 20000822
WO 2001-US40654 W 20010502

AB The present invention provides anti-inflammatory compds., pharmaceutical compns. thereof, and methods of use thereof for treating inflammatory disorders. The present invention also provides methods of identifying anti-inflammatory compds. and methods of inhibiting **NF-.kappa.**B-dependent target gene expression in a cell.

L118 ANSWER 13 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:300523 HCAPLUS
DOCUMENT NUMBER: 138:314539
TITLE: **TRAF6**-regulated **IKK** activators (TRIKA1 and TRIKA2) and their use as anti-inflammatory targets
INVENTOR(S): Chen, Zhijian J.; Deng, Li
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073097	A1	20030417	US 2001-76918	20011011

PRIORITY APPLN. INFO.: US 2001-76918 20011011

AB Proteins in the **IKK** and JNK signaling pathways, such as **NF**κ B, are involved in the regulation of inflammatory diseases. Through phosphorylation and polyubiquitination, IκB proteins which sequester **NF**κ B in the cytoplasm, are degraded by the ubiquitin-proteasome pathway releasing **NF**κ B to the nucleus where it is activated. The present invention provides methods utilizing the composition of proteins in the **IKK**, JNK and ubiquitin-proteasome pathways such as, TRAF6 or TRAF2 (E3-ubiquitin protein ligase), TRIKA1/Uev1A/Ubc13 complex (E2-ubiquitin conjugating enzyme), and TRIKA2/TAK1(protein kinase), in screening for candidate modulators involved in activation of the **IKK** and JNK pathways. The application further provides methods of utilizing the candidate modulators as drug therapeutics against inflammatory and immune diseases.

L118 ANSWER 14 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:58799 HCAPLUS
DOCUMENT NUMBER: 138:118536
TITLE: Human cDNAs for a **PYRIN**/NBS/LRR protein family and uses thereof, including treatment of apoptosis or inflammatory disorders
INVENTOR(S): Bertin, John; Wang, Weiye; Blatcher, Maria
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 103 pp., Cont.-in-part of U.S. Ser. No. 66,521.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003017983	A1	20030123	US 2002-124498	20020417
US 2003027757	A1	20030206	US 2002-66521	20020131

PRIORITY APPLN. INFO.: US 2001-265231P P 20010131
US 2001-318645P P 20010910
US 2002-66521 A2 20020131

AB Sequences for human PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, and PYRIN-11 polypeptides, proteins, and nucleic acid mols. are disclosed. In addition to isolated PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, and PYRIN-11 proteins, the invention further provides PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, and PYRIN-11 fusion proteins, antigenic peptides and anti-PYRIN-2, -PYRIN-3, -PYRIN-5, -PYRIN-6, -PYRIN-7, -PYRIN-8, -PYRIN-10, and -PYRIN-11 antibodies. The invention also provides PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, and PYRIN-11 nucleic acid mols., recombinant expression vectors containing a nucleic acid mol. of the invention, host cells into which the expression vectors have been introduced and non-human transgenic animals in which a PYRIN-2, PYRIN-3, PYRIN-5, PYRIN-6, PYRIN-7, PYRIN-8, PYRIN-10, or PYRIN-11 gene has been

introduced or disrupted. The invention claims diagnostic methods utilizing antibodies, nucleic acid primers and probes, test kits, and compns. of the invention. The invention further claims use of the PYRIN polypeptides for identifying binding compds., compds. that affect the activity of transcription factor **NF**-κ B, compds. that affect the expression or activity of PYRIN polypeptides, treatment of disorders associated with inappropriate apoptosis, and treatment of inflammatory disorders. PYRIN proteins of the invention are proteins with pyrin, NBD (nucleotide binding domain), and LRR (leucine-rich repeat) domains. Expression of PYRIN cDNAs in various tissues is analyzed. PYRIN-8 and CARD-5 proteins activate transcription factor **NF**-**kappa**.B activity through the **IKK** complex. Also, PYRIN-8 can activate caspase-1, and induction of IL-1β secretion by PYRIN-8/CARD-5 requires active caspase-1. The exptl. results suggest PYRIN-8 and similar proteins are involved in signal transduction pathways for apoptosis and inflammation.

L118 ANSWER 15 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:25811 HCAPLUS
DOCUMENT NUMBER: 139:46666
TITLE: **BMS**-345541 Is a Highly Selective Inhibitor of IκB Kinase That Binds at an Allosteric Site of the Enzyme and Blocks **NF**-**.kappa**.B-dependent Transcription in Mice
AUTHOR(S): Burke, James R.; Pattoli, Mark A.; Gregor, Kurt R.; Brassil, Patrick J.; MacMaster, John F.; McIntyre, Kim W.; Yang, Xiaoxia; Iotzova, Violetta S.; Clarke, Wendy; Strnad, Joann; Qiu, Yuping; Zusi, F. Christopher
CORPORATE SOURCE: Inflammation and Pulmonary Drug Discovery, Department of Immunology, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543, USA
SOURCE: Journal of Biological Chemistry (2003), 278(3), 1450-1456
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The signal-inducible phosphorylation of serines 32 and 36 of IκBα is critical in regulating the subsequent ubiquitination and proteolysis of IκBα, which then releases **NF**-**kappa**.B to promote gene transcription. The multisubunit IκB kinase responsible for this phosphorylation contains two catalytic subunits, termed IκB kinase (**IKK**)-1 and **IKK**-2. BMS-345541 (4(2'-aminoethyl)amino-1,8-dimethylimidazo(1,2-a)quinoxaline) was identified as a selective inhibitor of the catalytic subunits of **IKK** (**IKK**-2 IC50 = 0.3 μM, **IKK**-1 IC50 = 4 μM). The compound failed to inhibit a panel of 15 other kinases and selectively inhibited the stimulated phosphorylation of IκBα in cells (IC50 = 4 μM) while failing to affect c-Jun and STAT3 phosphorylation, as well as mitogen-activated protein kinase-activated protein kinase 2 activation in cells. Consistent with the role of **IKK**/**NF**-κ B in the regulation of cytokine transcription, BMS-345541 inhibited lipopolysaccharide-stimulated tumor necrosis factor α, interleukin-1β, interleukin-8, and interleukin-6 in THP-1 cells with IC50 values in the 1- to 5-μM range. Although a Dixon plot of the inhibition of **IKK**-2 by BMS-345541 showed a non-linear relationship indicating non-Michaelis-Menten kinetic binding, the use of multiple inhibition analyses indicated that BMS-345541 binds in a mutually exclusive manner with respect to a peptide inhibitor

corresponding to amino acids 26-42 of IκBα with Ser-32 and Ser-36 changed to aspartates and in a non-mutually exclusive manner with respect to ADP. The opposite results were obtained when studying the binding to **IKK**-1. A binding model is proposed in which BMS-345541 binds to similar allosteric sites on **IKK**-1 and **IKK**-2, which then affects the active sites of the subunits differently. BMS-345541 was also shown to have excellent pharmacokinetics in mice, and peroral administration showed the compound to dose-dependently inhibit the production of serum tumor necrosis factor α following i.p. challenge with lipopolysaccharide. Thus, the compound is effective against **NF-κ** B activation in mice and represents an important tool for investigating the role of **IKK** in disease models.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L118 ANSWER 16 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:453233 HCAPLUS
DOCUMENT NUMBER: 135:57859
TITLE: Cloning, sequencing and characterization of human **IKK4** kinase and use of the **IKK4** in screening for anti-inflammatory agents
INVENTOR(S): Hashimoto, Yasuhiro; Takemoto, Yoshihiro; Furuta, Masaaki; Sakai, Yutaka
PATENT ASSIGNEE(S): Glaxo Wellcome Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001044444	A2	20010621	WO 2000-JP8873	20001214
WO 2001044444	A3	20020510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-29542 A 19991214
AB A novel inhibitory κB kinase (**IKK**) is disclosed herein as **IKK4**. The full length **IKK4** cDNA was obtained by PCR from the human Jurkat cell line. The cDNA sequence of human **IKK4** reveals a 2187 bp open reading frame which encoded a 729 amino acid protein. **IKK4** is one of a critical kinases for the IL-8 gene regulation via the **NF-κ** B site. Polynucleotides encoding **IKK4**, expression vectors comprising said polynucleotides and screening methods for identifying therapeutic modulators of **IKK4** activity for treatment of conditions involving inflammation are also disclosed.

L118 ANSWER 17 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:80624 HCAPLUS
DOCUMENT NUMBER: 136:101079
TITLE: New **Ras**-like protein specifically

interacting with I-κB, inhibitor of **NF**-κ B
INVENTOR(S): Na, Doe Seon; Lee, Jae Un; Na, Sun Yeoung
PATENT ASSIGNEE(S): S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2000009513	A	20000215	KR 1998-29985	19980724

PRIORITY APPLN. INFO.: KR 1998-29985 19980724

AB PURPOSE: New Ras-like protein which interacts with I-κB, an inhibitor of **NF**-κ B, its gene and a separation method thereof from mice are provided which can be used as anti-inflammatory agent, immunomodulator, and anticancer drug. CONSTITUTION: New Ras-like protein which interacts with I-κB, an inhibitor of **NF**-.**kappa**.B is separated from mice by using a yeast 2 hybrid method, determining its gene base sequence and amino acid sequence and a characteristic inhibiting **NF**-κ B activation intermediated by TNFα or IL-1 is examined New Ras-like protein can be used for examining and searching a mechanism of **NF**-κ B or other signal transduction pathway. And this new Ras-like protein can be used as anti-inflammatory agent, immunomodulator, anticancer drug, and its search system. The identification of Ras-like protein interacting with I-κB by a glutathione S-transferase pull Down assay is shown in graph 2b.

L118 ANSWER 18 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:677038 HCAPLUS
DOCUMENT NUMBER: 133:347646
TITLE: **A20** and **A20**-binding proteins as cellular **inhibitors** of **nuclear factor-.kappa.B**-dependent gene expression and apoptosis
AUTHOR(S): Beyaert, R.; Heyninck, K.; Van Huffel, S.
CORPORATE SOURCE: Department of Molecular Biology, Unit of Molecular Signal Transduction in Inflammation, Ghent University and Flanders Interuniversity Institute for Biotechnology, Ghent, Belg.
SOURCE: Biochemical Pharmacology (2000), 60(8), 1143-1151
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 77 refs. Proper gene expression and cell growth are critical for the survival of all organisms. Nuclear factor-kappaB (**NF**-.**kappa**.B)-dependent gene expression and apoptosis play crucial roles in numerous cellular processes, and defects in their regulation may contribute to a variety of diseases including inflammation and cancer. Although there has recently been tremendous progress in our understanding of the signaling pathways that lead to **NF**-κ B activation and apoptosis, signaling mechanisms that neg. regulate these processes are only partially understood. This review deals with the zinc finger protein A20, which has been characterized as a dual inhibitor of **NF**-κ B activation and apoptosis. Its inducible expression by a wide variety of stimuli, including cytokines such as tumor necrosis factor, interleukin-1, and CD40, as well as bacterial and viral

products such as lipopolysaccharide, Epstein-Barr virus latent membrane protein 1, and human T-cell leukemia virus type I Tax, suggests that it is involved in the neg. feedback regulation of signaling. We will discuss the possible underlying mechanisms, placing emphasis on the role of several A20-binding proteins that have recently been described. Moreover, evidence is presented that A20 and A20-binding proteins are potential novel therapeutic tools in the treatment of a variety of diseases.
REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L118 ANSWER 19 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:511259 HCAPLUS
DOCUMENT NUMBER: 131:141477
TITLE: **NF-κ** B activation inhibitors, methods for screening the inhibitors using the function of **TGF-β** activated kinase 1 as parameter, and therapeutical use of the inhibitors for autoimmune diseases and inflammation
INVENTOR(S): Sugita, Takahisa; Sakurai, Hiroaki; Kageyama, Noriko; Hasegawa, Ko
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940202	A1	19990812	WO 1999-JP422	19990202
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9920764	A1	19990823	AU 1999-20764	19990202
JP 2000197500	A2	20000718	JP 1999-26803	19990204

PRIORITY APPLN. INFO.: JP 1998-26003 A 19980206
JP 1998-309316 A 19981030
WO 1999-JP422 W 19990202

AB Described is a method of identifying **nuclear factor . kappa.B** (**NF-κ** B) activation **inhibitors**, which have prophylactic and therapeutic uses for autoimmune diseases and inflammation, by testing whether a sample substance is able to inhibit the function of TGF-β activated kinase 1 (TAK1). The function of TAK1 is selected from (1) interaction between TAK1 and TAK1-binding protein 1 (TAB1); (2) protein kinase activity of TAK1; (3) TAK1-mediated intracellular activation of the IκB kinase (**IKK**) complex; and (4) TAK1-mediated **NF-.kappa** .B activation. The method was demonstrated using a yeast two-hybrid system (using the TAK1-TAB1 interaction as a marker and β-galactosidase a reporter).
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L118 ANSWER 20 OF 41 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:314897 HCAPLUS
DOCUMENT NUMBER: 131:142322

TITLE: Transcriptional regulation of **vascular endothelial** cell proteins
AUTHOR(S): Hofer, Erhard; De Martin, Rainer; Lipp, Joachim
CORPORATE SOURCE: Laboratory of Molecular Vascular Biology at Vienna International Research Cooperation Center Department of Vascular Biology and Thrombosis Research, University of Vienna, Vienna, Austria
SOURCE: NATO Science Series, Series A: Life Sciences (1999), 308(Vascular Endothelium: Mechanisms of Cell Signaling), 3-17
CODEN: NASAF2; ISSN: 1387-6686
PUBLISHER: IOS Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 83 refs., with focus on the major transcription factors interacting with regulatory promoter elements found in a number of genes induced by main triggers of the inflammatory and angiogenic response. Essential signals, proteins and functions which determine the inflammatory and angiogenic response are defined. Therapeutic approaches to prevent endothelial cell activation and to treat the corresponding diseases are discussed.
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L118 ANSWER 21 OF 41 EMBASE
on STN DUPLICATE 1
ACCESSION NUMBER: 2003268082 EMBASE
TITLE: Dominant-negative **I.kappa.B** facilitates apoptosis of osteoclasts by tumor necrosis factor-α.
AUTHOR: Abbas S.; Abu-Amer Y.
CORPORATE SOURCE: Y. Abu-Amer, Washington Univ. School of Medicine, Dept. of Orthopedic Surgery, Campus Box 8233, One Barnes Hospital Plaza, St. Louis, MO 63110, United States.
abuamery@msnotes.wustl.edu
SOURCE: Journal of Biological Chemistry, (30 May 2003) 278/22 (20077-20082).
Refs: 47
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Osteoclasts are the sole bone-resorbing cells. Heightened activity of these cells under pathological conditions leads to the development of bone loss diseases, such as osteolysis, osteoporosis, and rheumatoid arthritis. We have shown previously that tumor necrosis factor α-(TNF) strongly induces osteoclastogenesis of preosteoclasts and do so through activation of the transcription factor, **NF**-κ B. Most importantly, recent studies have shown that **NF-.kappa**.B is required for the development of osteoclasts. This transcription factor has also been proven as an essential mediator of inflammatory diseases including those related to bone. In this regard, we have shown that various mutated forms of **I.kappa.B** α are potent inhibitors of osteoclastogenesis. In this study, we examined the direct effect of DN-**I.kappa.B** on mature and preosteoclast development in the presence of TNF. Our findings indicate that once committed to the osteoclastogenic pathway,

preosteoclasts form giant and hyperactive osteoclasts in response to TNF. However, administration of DN-**I.kappa.B** to cultures prior to TNF exposure averts the osteoclastogenic effect of TNF into apoptosis. Screening potential mediators of DN-**I.kappa.B** and TNF-induced apoptosis shows that caspase 3, caspase 9, poly-(ADP-ribose)polymerase, and Bax are activated, whereas levels of Bcl-X(L), cIAP-1, and TRAF6 were reduced. Taken together, these findings suggest that under conditions of **NF-**κ B inactivity levels of pro-survival factors are diminished, which in turn facilitates TNF induction of pro-apoptotic factors leading to apoptosis.

L118 ANSWER 22 OF 41 EMBASE
on STN

ACCESSION NUMBER: 2001240863 EMBASE
TITLE: **NF-**K B in rheumatoid arthritis: A pivotal regulator of inflammation, hyperplasia, and tissue destruction.
AUTHOR: Makarov S.S.
CORPORATE SOURCE: S.S. Makarov, University of North Carolina, Center for Inflammatory Disorders, Thurston Arthritis Research Center, 4109 Thurston, Chapel Hill, NC 27599-7280, United States. smak@med.unc.edu
SOURCE: Arthritis Research, (2001) 3/4 (200-206).
Refs: 61
ISSN: 1465-9905 CODEN: ARRECG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The transcription factor **NF-**κ B has been well recognized as a pivotal regulator of inflammation in rheumatoid arthritis (RA), but recent developments revealed a broad involvement of **NF-**κ B in other aspects of RA pathology, including development of T helper 1 responses, activation, abnormal apoptosis and proliferation of RA fibroblast-like synovial cells, and differentiation and activation of bone resorbing activity of osteoclasts. In agreement with this, studies in animal models of RA have demonstrated the high therapeutic efficacy of specific inhibitors of **NF-.kappa**.B pathway, indicating the feasibility of anti-**NF-.kappa**.B therapy for human disease.

L118 ANSWER 23 OF 41 EMBASE
on STN

ACCESSION NUMBER: 2000297995 EMBASE
TITLE: **Phorbol** esters and cytokines regulate the expression of the **NEMO**-related protein, a molecule involved in a **NF-.kappa**.B-independent pathway.
AUTHOR: Schwamborn K.; Weil R.; Courtois G.; Whiteside S.T.; Israel A.
CORPORATE SOURCE: A. Israel, Unite Biol. Molec. Express. Genique, URA 1773 CNRS, Institut Pasteur, 25 Rue du Dr. Roux, 75724 Paris Cedex 15, France. aisrael@pasteur.fr
SOURCE: Journal of Biological Chemistry, (28 Jul 2000) 275/30 (22780-22789).
Refs: 34

ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The **NF-κ** B signaling pathway plays a crucial role in the immune, inflammatory, and apoptotic responses. Recently, we identified the **NF-κ** B **Essential Modulator** (**NEMO**) as an essential component of this pathway. **NEMO** is a structural and regulatory subunit of the high molecular kinase complex (**IKK**) responsible for the phosphorylation of **NF-κ** B inhibitors. Data base searching led to the isolation of a cDNA encoding a protein we called NRP (**NEMO**-related protein), which shows a strong homology to **NEMO**. Here we show that NRP is present in a novel high molecular weight complex, that contains none of the known members of the **IKK** complex. Consistently, we could not observe any effect of NRP on **NF-κ** B signaling. Nonetheless, we could demonstrate that treatment with phorbol esters induces NRP phosphorylation and decreases its half-life. This phosphorylation event could only be inhibited by K-252a and stauroporin. We also show that de novo expression of NRP can be induced by interferon and tumor necrosis factor α and that these two stimuli have a synergistic effect on NRP expression. In addition, we observed that endogenous NRP is associated with the Golgi apparatus. Analogous to **NEMO**, we find that NRP is associated in a complex with two kinases, suggesting that NRP could play a similar role in another signaling pathway.

L118 ANSWER 24 OF 41 EMBASE
on STN

ACCESSION NUMBER: 2000103493 EMBASE
TITLE: The **I.kappa.B/NF-.kappa.B** system: A key determinant of **mucosal** inflammation and protection.
AUTHOR: Jobin C.R.; Sartor R.B.
CORPORATE SOURCE: C.R. Jobin, Div. of Digestive Dis. and Nutrition, CB 7038, Univ. of North Carolina, Chapel Hill, NC 27599-7038, United States. Job@med.unc.edu
SOURCE: American Journal of Physiology - Cell Physiology, (2000) 278/3 47-3 (C451-C462).
Refs: 137
ISSN: 0363-6143 CODEN: AJPCDD
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The ubiquitous transcription factor **NF-κ** B is a central regulator of the transcriptional activation of a number of genes involved in cell adhesion, immune and proinflammatory responses, apoptosis, differentiation, and growth. Induction of these genes in intestinal epithelial cells (IECs) by activated **NF-.kappa.B** profoundly influences mucosal inflammation and repair. **NF-κ** B activation requires the removal of **I.kappa.B** from **NF-κ** B by inducible proteolysis, which liberates this transcription factor for migration to the nucleus, where it binds to κB-regulatory elements and induces transcription. **I.kappa.B**.alpha. degradation is incomplete and delayed in IECs, resulting in buffered

responses to luminal stimuli. The stimulatory environment partially determines whether the effect of **NF**-κ B is protective or deleterious for the host. κB-dependent proinflammatory gene expression, particularly chemokines, major histocompatibility complex class II antigens, and adhesion molecules may be extremely important in early protective responses to mucosal pathogens but, when dysregulated, could lead to the development of chronic inflammation, as seen in inflammatory bowel diseases. The key role of **NF-.kappa** .B in regulating expression of a number of proinflammatory genes makes this protein an attractive target for selective therapeutic intervention.

L118 ANSWER 25 OF 41 EMBASE
on STN

ACCESSION NUMBER: 1999241157 EMBASE
TITLE: Required and nonessential functions of nuclear factor-kappa B in bone cells.
AUTHOR: Boyce B.F.; Xing L.; Franzoso G.; Siebenlist U.
CORPORATE SOURCE: Dr. B.F. Boyce, Department of Pathology, University of Texas, Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284, United States. boyce@uthscsa.edu
SOURCE: Bone, (1999) 25/1 (137-139).
Refs: 34
ISSN: 8756-3282 CODEN: BONEDL
PUBLISHER IDENT.: S 8756-3282(99)00105-2
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Nuclear factor-kappa B (**NF**-κ B) is a set of five polypeptide transcription factors, called p50, p52, p65 (also called Rel A), Rel B, and c-Rel, which regulate the expression of a variety of genes involved in immune and inflammatory responses. They were originally named because they were considered essential regulators of B cell kappa light chain expression. More recent studies indicate that **NF-**. **kappa**.B proteins are involved in the regulation of a variety of other cell functions, including cell proliferation, responses to stress, and apoptosis. **NF**-κ B heterodimers reside in the cytoplasm of cells bound to inhibitory proteins, the two commonest of which are **I**.**kappa**.**B**.alpha. and **I**. **kappa**.**B**.beta., which prevent **NF-.kappa** .B from entering the nucleus. When cells are stimulated, **I**. **kappa**.**B** is phosphorylated by specific **I**. **kappa**.**B** kinases and subsequently is ubiquitinated and degraded in proteosomes. This allows **NF**-κ B to translocate to the nucleus to regulate the expression of a growing list of genes, including the proinflammatory cytokines, interleukin-1 (IL-1), IL-6, and tumor necrosis factor. IL-1 and tumor necrosis factor in turn also regulate the expression of **NF**-κ B. Thus, once activated, **NF**-κ B may be involved in upregulatory loops, which can amplify the effects of the initiating stimulus. Because these proinflammatory cytokines have been implicated in the pathogenesis of estrogen deficiency and inflammation-related bone loss, it is likely that **NF**-κ B has a significant role in the increased generation and function of osteoclasts in these circumstances. However, an unexpected and essential role of **NF-**. **kappa**.B in the formation of osteoclasts during development was discovered recently after the generation of knockout mice, which lack the expression of the p50 and p52 subunits. This paper will describe recent

studies that reveal an essential role for **NF-κ** B signaling in the generation of osteoclasts and that suggest that **NF-κ** B may also play a key central role in the activation and survival of osteoclasts in conditions in which osteoclastogenesis is upregulated.

L118 ANSWER 26 OF 41 EMBASE
on STN

ACCESSION NUMBER: 97295985 EMBASE
DOCUMENT NUMBER: 1997295985
TITLE: Genetic approaches to study Rel/**NF-.kappa** .B/**I.kappa.B** function in mice.
AUTHOR: Attar R.M.; Caamano J.; Carrasco D.; Iotsova V.; Ishikawa H.; Ryseck R.-P.; Weih F.; Bravo R.
CORPORATE SOURCE: R.M. Attar, Department of Oncology, Bristol-Myers Squibb Pharm Res Inst, PO Box 4000, Princeton, NJ 08543-4000, United States
SOURCE: Seminars in Cancer Biology, (1997) 8/2 (93-101).
Refs: 39
ISSN: 1044-579X CODEN: SECBE7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The generation of animal models in which individual members of a gene family are genetically altered is a particularly attractive way to elucidate their function. Members of the Rel/**NF-.kappa** .B/**I.kappa.B** family constitute an important network of transcription factors and regulatory proteins that control the expression of numerous cellular and viral genes crucial for a variety of processes. A few examples are developmental pattern formation and immune response in Drosophila, viral replication, and immune, inflammatory, acute phase and stress responses in vertebrates. The findings from knockout and transgenic mice developed to study Rel/**NF-κ** B/**I.kappa.B** function in vivo are reviewed here. In general, these studies point to the essential role of these factors in the development and function of the vertebrate immune system.

L118 ANSWER 27 OF 41 BIOSIS on STN

ACCESSION NUMBER: 2003:10134 BIOSIS
DOCUMENT NUMBER: PREV200300010134
TITLE: Demonstration of an activation regulated **NF-kappaB**/I-kappaBalpha complex in human **platelets.**
AUTHOR(S): Liu, Fengqi; Morris, Steve A.; Epps, Jerry L.; Carroll, Roger C. [Reprint Author]
CORPORATE SOURCE: Department of Anesthesiology, Graduate School of Medicine, University of Tennessee Medical Center, 1924 Alcoa Highway, Knoxville, TN, 37920, USA
rccarrol@mc.utmck.edu
SOURCE: Thrombosis Research, (May 15, 2002) Vol. 106, No. 4-5, pp. 199-203. print.
CODEN: THBRAA. ISSN: 0049-3848.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Dec 2002
Last Updated on STN: 18 Dec 2002

AB In eukaryotic cells, the ubiquity of the signaling system of

transcription factor nuclear factor-kappa B (**NF -kappaB**)/**I-kappa B** (I-kappaB) is undisputed. Numerous studies have reported that the **NF-kappaB**/I-kappaB complex plays a pivotal role in **regulating gene expression** controlling cell differentiation, cell proliferation, **inflammation**, oncogenesis, and apoptosis. Here we show that **NF-kappaB**/I-kappaB families exist in human platelets, natural anuclear corpuscles derived from megakaryocytes. Moreover, the I-kappaB kinase (**IKK**) is present and may phosphorylate I-kappaB during platelet activation. Coupled with intracellular calcium flux, this leads to I-kappaB dissociation from the **NF-kappaB**/I-kappaB complex and proteolysis. The **NF-kappaB**/I-kappaB proteins may have function independent of gene regulation in platelets.

L118 ANSWER 28 OF 41 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:48300 BIOSIS
DOCUMENT NUMBER: PREV199900048300
TITLE: Glutathione downregulates the phosphorylation of IbetaB: Autoloop regulation of the **NF-KAPPAB** -mediated expression of **NF-kappaB** **subunits** by TNF-alpha in mouse vascular endothelial cells.
AUTHOR(S): Cho, Sungsam; Urata, Yoshishige; Iida, Tetsuya; Goto, Shinji; Yamaguchi, Michiko; Sumikawa, Koji; Kondo, Takahito [Reprint author]
CORPORATE SOURCE: Dep. Biochemistry Molecular Biology Disease, Atomic Bomb Disease Institute, Nagasaki University School Medicine, Nagasaki 852-8523, Japan
SOURCE: Biochemical and Biophysical Research Communications, (Dec. 9, 1998) Vol. 253, No. 1, pp. 104-108. print. CODEN: BBRCA9. ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Feb 1999
Last Updated on STN: 10 Feb 1999

AB Nuclear factor-kappa B (**NF-kappaB**) **regulates gene expression** upon immune and **inflammatory** responses. It has been demonstrated that redox regulation by thiols is involved in the signal-transduction cascade. In this study, we examined the effect of glutathione (GSH) on the **NF-kappaB** activity and the expression of **NF-kappaB** subunits induced by tumor necrosis factor-alpha (TNF-alpha) using mouse vascular endothelial cells. GSH inhibited the serine phosphorylation of IkappaB-alpha by TNF-alpha, leading to the downregulation of **NF-kappaB**-DNA binding activity followed by decreased expression of p65/p50 and IkappaB mRNAs. The regulation of the autoregulatory loop for the **NF-kappaB** activation and the expression of **NF-kappaB** subunits may be important in endothelial cells in response to cytokines.

L118 ANSWER 29 OF 41 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:391477 BIOSIS
DOCUMENT NUMBER: PREV199799690680
TITLE: The role of nuclear factor-kappa-B in **cytokine** gene regulation.
AUTHOR(S): Blackwell, Timothy S. [Reprint author]; Christman, John W.
CORPORATE SOURCE: Div. Allergy, Pulmonary Critical Care Med., Vanderbilt Univ. Sch. Med., T-1217 MCN, Nashville, TN 27232-2650, USA
SOURCE: American Journal of Respiratory Cell and Molecular Biology, (1997) Vol. 17, No. 1, pp. 3-9.

Prepared by Toby Port 308-3534, Biotech Library

CODEN: AJRBEL. ISSN: 1044-1549.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Sep 1997
Last Updated on STN: 10 Sep 1997

AB **Transcription factors** are DNA-binding proteins that **regulate gene expression**. Nuclear factor-kappa-B (**NF-kappa**-B) is a critical **transcription factor** for maximal expression of many cytokines that are involved in the pathogenesis of **inflammatory** diseases, such as adult respiratory distress syndrome (ARDS) and sepsis syndrome. Activation and regulation of **NF-kappa**-B are tightly controlled by a group of inhibitory proteins (**I-kappa-B**) that sequester **NF-kappa**-B in the cytoplasm of immune/**inflammatory** effector cells. **NF-kappa**-B activation involves signaled phosphorylation, ubiquitination, and proteolysis of **I-kappa-B** . Liberated **NF-kappa**-B migrates to the nucleus, where it binds to specific promoter sites and activates gene transcription. The activation of **NF-kappa**-B initiates both extracellular and intracellular regulatory events that result in autoregulation of the **inflammatory** cascade through modulation of **NF-kappa**-B activation. Recently, activation of **NF-kappa**-B has been linked to ARDS and has been shown to be a critical proximal step in the initiation of neutrophilic **inflammation** in animal models. Activation of **NF-kappa**-B can be inhibited in vivo by treatment with antioxidants, corticosteroids, and the induction of endotoxin tolerance. Identification of more specific and efficacious inhibitors of **NF-kappa** -B activation might prove beneficial for the treatment of cytokine-mediated **inflammatory** diseases.

L118 ANSWER 30 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-493262 [46] WPIDS
DOC. NO. CPI: C2003-132040
TITLE: New **aminopyridines** and pyridines useful for treating e.g. **inflammatory**, metabolic or malignant conditions.
DERWENT CLASS: B02 B03
INVENTOR(S): HAWLEY, R C; LABADIE, S S; SJOGREN, E B; TALAMAS, F X
PATENT ASSIGNEE(S): (SYNT) SYNTEX USA LLC; (HOFF) HOFFMANN LA ROCHE & CO AG F
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003040131	A1	20030515	(200346)*	EN	98
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW					
US 2003144303	A1	20030731	(200354)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003040131	A1	WO 2002-EP12164	20021031

Prepared by Toby Port 308-3534, Biotech Library

US 2003144303 A1 Provisional US 2001-338312P 20011107
US 2002-288968 20021106

PRIORITY APPLN. INFO: US 2001-338312P 20011107; US 2002-288968 20021106

AB WO2003040131 A UPAB: 20030719

NOVELTY - Aminopyridines and pyridines are new.

DETAILED DESCRIPTION - Aminopyridines and pyridines of formula (I) are new.

V' or X = N or CRa;

Ra = H, 1-6C alkyl, 3-7C cycloalkyl or 3-7C cycloalkyl(1-6C)alkyl;

Y = O, S or NR;

R = CN, NO2 or T;

T = H, 1-10C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-(1-6C)alkyl, 3-10C alkenyl or 2-10C alkynyl;

Z = H, 1-6C alkyl, 3-7C cycloalkyl, 3-6C cycloalkyl-(1-6C)alkyl, 2-6C alkenyl, 2-6C alkynyl or N(R2)(R3);

R1 = T, 1-10C heteroalkyl, heterocyclyl, heterocyclyl(1-6C)alkyl, aryl, aryl(1-4C)alkyl, aryl(1-4C)heteroalkyl, heteroaryl(1-4C)alkyl, heteroaryl(1-4C)heteroalkyl, -C(O)R11 or 1-6C alkylene-C(O)R11;

R11 = H, 1-6C alkyl or NR12R13;

R12, R13 = H, 1-6C alkyl or 1-6C heteroalkyl;

R2, R3 = T or 1-10C heteroalkyl;

R2+R3 = 5 - 7-membered heterocyclyl ring;

R4 = H, 1-6C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-(1-6C)alkyl, 2-6C alkenyl or 2-6C alkynyl;

A = T, 1-10C heteroalkyl, heterocyclyl, heterocyclyl(1-6C)alkyl, heterosubstituted(3-7C)cycloalkyl, aryl, aryl(1-4C)alkyl, aryl(1-4C)heteroalkyl, heteroaryl, heteroaryl(1-4C)alkyl, heteroaryl(1-4C)heteroalkyl or R'aR'bNC(=X)-;

R'a, R'b = H, 1-4C alkyl or aryl;

X = O or S;

B' = 5- - 6-membered aromatic ring containing at least one N and 0 - 3 heteroatoms and optionally substituted by halo, CF3, CF3O, 1-6C alkyl, amino, mono or di-1-6C alkylamino, cyano, nitro, sulfonamido, acyl, acylamino or carboxamido;

U' = -NR5-, -O- or -S-; and

R5 = H or 1-6C alkyl.

Provided that one of either V' or X is N and the other is CRa, or both V and X are CRa.

INDEPENDENT CLAIMS are included for following:

(1) use of (I) in the manufacture of medicament for treating **inflammatory**, metabolic or malignant conditions; and

(2) preparation of (I);

(3) a pyridine derivative of formula (i).

ACTIVITY - **Antiinflammatory**; Antirheumatic; Antiarthritic; Gastrointestinal.; Antipsoriatic; Cytostatic; Antidiabetic; Antibacterial; Immunosuppressive; Antiulcer; Dermatological; Antiallergic; Antiasthmatic; Osteopathic; Nootropic; Neuroprotective; Nephrotropic; Antiarteriosclerotic; Cerebroprotective; Antibacterial; Antigout; Ophthalmological; Auditory; Respiratory; Vasotropic; Cytostatic.

MECHANISM OF ACTION - IkappaB kinases inhibitor; **NF-kappa** modulator.

96 well polystyrene microtiter plates were coated with Neutravidin (10 micro g/ml in phosphate buffered saline (PBS)). The coating solution was removed and in 80 micro l/well a kinase reaction mixture was added using a biotinylated substrate peptide (Lys-Lys-Glu-Arg-Leu-Leu-Asp-Asp-Arg-his-Asp-Ser-Gly-Leu-Asp-Ser-Met-Lys-Asp-Glu-Glu-Tyr-Glu-Gln-Gly-Lys bio, sequence derived from IkappaB- alpha). 1-(2-Butylamino-6-(3-methyl-3H-imidazol-4-yl)-pyrimidin-4-ylmethylene)-amino-1-methyl-thiourea (A) (1

nM - 30 micro M) was added in dimethylsulfoxide (DMSO) (10 micro 1/well). Recombinant full-length **IKK** beta enzyme was added in a buffer (10 micro 1) containing Tris-HCl pH 7.5 (20 mM), EGTA (2 mM), benzamidine (0.5 mM), DTT (1 mM), NP-40 (0.1 %), MgCl2 (10 mM) to initiate the kinase reaction. The reaction mixture was incubated at room temperature for 45 minutes. The reaction was then terminated. A conventional chemilumininescent ELISA detection technique was initiated and the IC50 value was determined. (A) showed IC50 value of 0.314 micro M.

USE - In the manufacture of a medicament for treating **inflammatory**, metabolic or malignant conditions e.g. rheumatoid arthritis, **inflammatory** bowel disease, psoriasis, cancer, diabetes and septic shock (all claimed). Also useful for treating systemic anaphylaxis; hypersensitivity responses; drug allergies; insect sting allergies; **inflammatory** bowel disease e.g. Crohn's disease, ulcerative colitis, ileitis and enteritis; vaginitis, psoriasis, **inflammatory** dermatoses e.g. dermatitis, eczema, atopic dermatitis, urticaria, vasculitis, spondyloarthropathies, scleroderma; respiratory allergies diseases e.g. asthma, allergic rhinitis, hypersensitivity lung disease; autoimmune disease e.g. arthritis (rheumatoid and psoriatic), osteoarthritis, multiple sclerosis, systemic lupus erythematosus, diabetes mellitus, glomerulonephritis; graft rejection e.g. allograft rejection and graft versus host disease; atherosclerosis, myositis; neurological conditions e.g. stroke and closed-head injuries, neurodegenerative diseases, Alzheimer's disease, encephalitis, meningitis, osteoporosis, gout, hepatitis, nephritis, sepsis, sarcoidosis, conjunctivitis, otitis, chronic obstructive pulmonary disease, sinusitis and Behcet's syndrome; neoplastic disease e.g. solid tumors (e.g. non-Hodgins lymphoma), skin cancer, melanoma, lymphoma and diseases in which angiogenesis and neovascularization play a role.

ADVANTAGE - The compounds inhibit IkB kinases.

Dwg.0/0

L118 ANSWER 31 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-093119 [08] WPIDS
DOC. NO. CPI: C2003-023365
TITLE: Novel **NF-kappaB**-associated polypeptides and polynucleotides useful for diagnosing, treating and preventing cancer, hepatic disorders, aberrant apoptosis, viral infections, autoimmune disorders, asthma and stroke.
DERWENT CLASS: B04 D16
INVENTOR(S): CARMAN, J; FEDER, J; NADLER, S
PATENT ASSIGNEE(S): (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002086076	A2	20021031	(200308)*	EN	608

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2002086076 A2 WO 2002-US12636 20020419

PRIORITY APPLN. INFO: US 2002-346986P 20020109; US 2001-284962P 20010419; US 2001-286645P 20010426

AB WO 200286076 A UPAB: 20030204

NOVELTY - An isolated **NF-kappaB**-associated polypeptide (I) comprising a polypeptide fragment, domain, epitope, full length protein, variant, allelic variant or species homolog of any of 23 113-787 residue amino acid sequences (S1), given in the specification, is new. The polypeptide fragment is capable of modulating an **NFkappaB** response.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid molecule (II) comprising a polynucleotide fragment comprising any of 142 90-5085 nucleotide sequences, given in the specification, a polynucleotide encoding (I), which is hybridizable to S2 and having **NF-kappaB** modulating activity, a polynucleotide which represents the complementary sequence (antisense) of S2, a polynucleotide capable of hybridizing under stringent conditions to any one of the above polynucleotides, where the polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A or T residues;

(2) an antibody (Ab) that binds specifically to (I);

(3) identifying or screening for a compound that modulates the biological activity of **NF-kappaB** associated molecule; and

(4) a compound (C) that modulates the biological activity of a human **NF-kappaB** associated molecule as identified by the method of (3).

ACTIVITY - **Antiinflammatory**; Cytostatic; Hepatotropic; Virucide; Anti-HIV (human immunodeficiency virus); Antirheumatic; Antiarthritic; Antiasthmatic; Immunomodulator; Antidiabetic; Antiallergic; Neuroprotective; Immunosuppressive; Vulnerary; Antibacterial; Antiinfertility; Antianemic; Antipsoriatic; Cerebroprotective; Cardiant; Antiarteriosclerotic.

MECHANISM OF ACTION - Vaccine; Gene therapy; Inhibitor of tumor necrosis factor (TNF) alpha -induced adhesion molecule expression; Modulator of IkappaB phosphorylation; Modulator of **IKK**-1, **IKK**-2 or **IKK**- gamma activity; Modulator of cytokine activity. No biological data is given.

USE - (I) is useful for preventing, treating or ameliorating a medical condition (MC) e.g. immune disorder, **inflammatory** disorders in which (I) are associated with the disorder either directly or indirectly, an **inflammatory** disorder related to aberrant **NF-kappaB** regulation, cancer, aberrant apoptosis, hepatic disorders, Hodgkin's lymphomas, hematopoietic tumor, hyper-IgM syndromes, hypohydrotic ectodermal dysplasia, X-linked anhidrotic ectodermal dysplasia, immunodeficiency, al incontinentia pigmenti, viral infections, human immunnodeficiency virus (HIV)-1, human T-cell lymphotropic virus (HTLV)-1, hepatitis B, hepatitis C, Epstein Barr virus (EBV), influenza, viral replication, host cell survival and evasion of immune responses, rheumatoid arthritis, **inflammatory** bowel disease, colitis, asthma, atherosclerosis, cachexia, euthyroid sick syndrome, stroke, experimental allergic encephalomyelitis (EAE), autoimmune disorders, disorders related to hyper immune activity, disorders related to aberrant acute phase responses, hypercongenital conditions, birth defects, necrotic lesions, wounds, organ transplant rejection, conditions related to organ transplant rejection, disorders related to aberrant signal transduction, proliferating disorders, cancers and HIV propagation in cells infected with other viruses. (I) or (II) is

useful for diagnosing a **NF-kappaB** associated condition or a susceptibility to a **NF-kappaB** associated condition e.g. MC, by determining the presence or amount of expression of (I) in a biological sample, or determining the presence or absence of a mutation in (II) and diagnosing **NF-kappaB** associated condition based on the presence of mutation which indicates predisposition to **NF-kappaB** associated condition. (I) is useful for identifying a binding partner to (I), that effects an activity of (I). (I) or (II) is also useful for identifying a compound that modulates the biological activity of **NF-kappaB** associated molecule.
(All claimed.) (I) is useful as molecular weight markers, to raise antibodies and to assess various biological activities. (II) is useful in interaction trap assays, in chromosome identification, in gene therapy, for identifying organisms from minute biological samples and as an alternative to Restriction Fragment Length Polymorphism (RFLP) and as molecular weight markers. (I) and (II) are useful as probes for the identification and isolation of full-length cDNAs and/or genomic DNAs corresponding to (II), as probes to hybridize and discover novel DNA, for positional cloning of related sequences, to subtract-out known sequences in the process of discovering other novel polynucleotides, in microarrays and to quantify gene expression. (I) and (II) are also useful for treating diseases of pancreas e.g. diabetes mellitus, vitamin B12 malabsorption and other genetic syndromes associated with diabetes mellitus such as Huntington's chorea and Turner's syndrome, bacterial infections, cardiovascular disorders, infertility, psoriasis and hemolytic anemia. (I) and (II) are also useful for modulating hemostatic or thrombolytic activity, modulating epithelial cell proliferation, stimulating neuronal growth, stimulate growth and differentiation of hematopoietic cells and bone marrow cells, inducing tissue of mesodermal origin, modulating mammalian characteristics, for treating hyperproliferative disorders, diseases at cellular level, neurological diseases, infectious diseases, as food additives and preservatives, to increase the efficacy of pharmaceutical preparations and to prepare individuals to altered environmental conditions such as extraterrestrial level. Ab is useful for detecting, isolating, purifying and targeting (I), and in immunoassays for qualitatively and quantitatively measuring (I) in biological samples. Ab is also useful in immunophenotyping of cell lines and biological samples.
Dwg.0/79

L118 ANSWER 32 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-698429 [75] WPIDS
DOC. NO. CPI: C2002-197663
TITLE: New 4-aryl pyridine derivatives useful for the treatment of diseases associated with nuclear factor **kappa B** activity.
DERWENT CLASS: B03
INVENTOR(S): FUCHIKAMI, K; IKEGAMI, Y; KOMURA, H; LOWINGER, T B; MASUDA, T; MURATA, T; SAKAKIBARA, S; SHIMADA, M; SHIMAZAKI, M; SHINTANI, T; UMEDA, M; YOSHIDA, N; YOSHINO, T; ZIEGELBAUER, K B
PATENT ASSIGNEE(S): (FARB) BAYER AG
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002044153	A1	20020606	(200275)*	EN	113

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR

KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
AU 2002031628 A 20020611 (200275)
JP 2002193938 A 20020710 (200275) 157
EP 1339687 A1 20030903 (200365) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002044153	A1	WO 2001-EP13338	20011119
AU 2002031628	A	AU 2002-31628	20011119
JP 2002193938	A	JP 2000-366708	20001201
EP 1339687	A1	EP 2001-991731	20011119
		WO 2001-EP13338	20011119

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002031628	A	Based on	WO 2002044153
EP 1339687	A1	Based on	WO 2002044153

PRIORITY APPLN. INFO: JP 2000-366708 20001201
AB WO 200244153 A UPAB: 20021209
NOVELTY - 4-Aryl pyridine derivatives are new.
DETAILED DESCRIPTION - 4-Aryl pyridine derivatives of formula (I) or its salt are new.
X = CH or N;
R1 = H, OH, halo, 1-6C alkyl, 1-6C alkoxy, 1-6C alkoxy-carbonyl, nitro, amino, mono- or di-(1-6C alkyl)amino, phenylsulfonylamino, -NHR11 or -O-(CH2)n-R12;
R11 = 1-6C alkyl, 1-6C alkanoyl or 1-6C alkyl-sulfonyl (all substituted by phenyl);
n = 0-6;
R12 = 2-6C alkenyl, benzoyl, mono or di phenyl, mono or di(1-6C alkyl)amino, 1-6C alkanoyl, 1-6C alkoxycarbonyl or 3-10 membered optionally saturated ring (containing 0-3 S, O and/or N and optionally substituted by OH, nitro, cyano, mono- or di-halo, 1-6C alkyl (optionally substituted by halo), amino, mono or di-(1-6C alkyl)amino, 1-6C alkanoylamino, carbamoyl, 1-6C alkoxy, 1-6C alkoxycarbonyl, or phenyl);
R2 = H, OH, halo or 1-6C alkyl;
R3 = H, OH, halo, 1-6C alkoxy, 1-6C alkyloxy (substituted by 3-6C cycloalkyl), -NR31R32 or 3-6 membered saturated ring (containing 0-3 O or N and optionally substituted by R33);
R31, R33a = H or 1-6C alkyl;
R32 = H, 1-6C alkanoyl, 1-6C alkyl (optionally substituted by OH or phenyl);
R33 = nitro, cyano, 1-6C alkyl (optionally substituted by OH or amino), 1-6C alkoxy, 1-6C alkyloxy (substituted by OH and amino), 1-6C alkanoyl, carbamoyl or -NR33aR33b;
R33b = H, 1-6C alkyl (optionally substituted by OH or phenyl), 1-6C alkanoyl, 1-6C alkylsulfonyl or trifluoroacetyl;
R4 = H, OH, carboxy, -CO-NHR41, amino, 1-6C alkylsulfonylamine, -NH-COR41 or 1-6C alkyl (optionally substituted by R42, 1-6C alkoxy, R43-1-6C alkyloxy);
R41 = 1-6C alkyl (optionally substituted by R41a), 1-6C alkoxy, oxotetrahydrofuryl, oxopyrrolidinyl, -CH(OH)R41b, -CH(NH2)R41c, -NHR41c or piperazine (optionally substituted by R41d);

R41a = carboxy, 1-6C alkoxy, -CH(NH2)carboxy, -NR41a'R41a'' or 3-10 membered saturated ring (containing 0-3 O or N and optionally substituted by carboxy, 1-6C alkyl (optionally substituted by OH or benzodioxane), 3-6C cycloalkyl, 1-6C alkanoyl, carboxy, benzyl, 1-6C alkoxycarbonyl or furoyl);

R41a' = H or 1-6C alkyl (optionally substituted by OH, 1-6C alkyloxy, 3-8C cycloalkyl or piperidino);

R41a'' = H, 1-6C alkyl (optionally substituted by OH, 1-6C alkyloxy or 3-6C cycloalkyl), 1-6C alkoxy or 3-6 membered saturated ring (containing 0-3 O or N and optionally substituted by carboxy, 1-6C alkyl, 1-6C alkanoyl or 1-6C alkyloxy);

R41b = 1-6C alkyl (optionally substituted by carboxy), 1-6C alkyloxy, 1-6C alkoxy or 1-6C alkoxycarbonyl;

R41c = carboxy, 1-6C alkyl (optionally substituted by carboxy) or 3 - 6 membered saturated ring (containing 0 - 3 heteroatoms selected from O or N);

R41d = 1-6C alkyl (optionally substituted by carboxy) or 1-6C alkyloxy or 1-6C alkoxy;

R42 = T or 1-6C alkoxy;

T = carboxy, amino, -CH(NH2)-carboxy or 5-7 membered optionally saturated ring (containing 0-3 O or N and optionally substituted by OH, nitro, mono- or di-halo, 1-6C alkyl (optionally substituted by halo), amino, mono or di(1-6C alkyl)amino or carbamoyl);

R43 = T;

R3+R4 = 4-6 membered saturated ring (containing 0-3 O or N and optionally substituted by at least one OH, nitro, mono- or dihalo, 1-6C alkyl (optionally substituted by halo), oxo, amino, mono or di (1-6C alkyl)amino or carbamoyl);

R5 = H, cyano, carboxy, carbamoyl, 1-6C alkyl (optionally substituted by OH or carbamoyl) or 1-6C alkoxycarbonyl;

R6 = -NR61R62;

R61 = H or 1-6C alkyl;

R62 = H, 1-6C alkyl, phenyl, benzyl or 1-6C alkanoyl;

NR61R62 = 5-6 membered ring (optionally containing NH or O);

R5+R6 = 5-7 membered optionally saturated ring (containing 0-3 O, S or N and optionally substituted by halo, nitro, cyano, oxo, thioxo, 1-6C alkyl, 1-6C alkylsulfonyl, 1-6C alkoxy, 1-6C alkoxycarbonyl, phenyl, 1-6C alkanoyl, amino, 1-6C alkylamino, 1-6C alkanoylamino, carbamoyl, 3-8C cycloalkylaminocarbonyl, 1-6C alkylaminocarbonyl, 1-6C alkylaminocarbonyl (substituted by halo), di(1-6C alkyl)aminocarbonyl, benzoylamino, phenylsulfonyl, di(1-6C alkyl)amino-1-6C alkylaminocarbonyl, hydroindenylaminocarbonyl, diphenylmethylaminocarbonyl, pyrrolidinocarbonyl, 1-6C alkyloxy-1-6C alkyl amino carbonyl, morpholinocarbonyl, piperazinocarbonyl, phenyl-1-6C alkylaminocarbonyl, carboxy-1-6C alkylaminocarbonyl, 3-8C cycloalkyl-1-6C alkylaminocarbonyl, hydroxy-1-6C alkylaminocarbonyl or methylsulfonylaminocarbonyl.

An INDEPENDENT CLAIM is included for use of (I) in the production of medicament for controlling inflammatory disorders.

ACTIVITY - Antiinflammatory; Antiasthmatic; Antiallergic; Dermatological; Immunosuppressive; Antipsoriatic; Antibacterial; Antigout; Vasotropic; Cytostatic.

MECHANISM OF ACTION - IkB kinase beta inhibitor; Nuclear factor kappa B inhibitor; Cytokine inhibitor.

USE - For the control of inflammatory disorders; as an IkB kinase beta (IKK- beta)inhibitor; as an anti-inflammatory agent to treat asthma, allergic rhinitis, atopic dermatitis, hives, conjunctivitis, vernal catarrh, chronic arthrorheumatism, systemic lupus erythematosus, psoriasis, diabrotic colitis, systemic inflammatory response syndrome (SIRS), sepsis, polymyositis, dermatomyositis (DM), polyarthritis nodosa (PN), mixed connective tissue disease (MCTD), Sjoegren's syndrome and gout; as an immunosuppressant; to treat ischemia; and as an anti-tumor

agent (all claimed).
ADVANTAGE - The compounds show excellent selectivity and strong activity in vivo assays and unexpectedly excellent NF-kappaB inhibitory activity based on IKK- beta inhibition and cytokine inhibition.
Dwg.0/0

L118 ANSWER 33 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-471256 [50] WPIDS
DOC. NO. CPI: C2002-133946
TITLE: Novel isolated PAAD domain containing polypeptide useful for inducing apoptosis by inhibiting nuclear factor **kappa B** activation and in gene therapy for treating cancer.
DERWENT CLASS: B04 D16
INVENTOR(S): ARIZA, M E; CHU, Z; FIORENTINO, L; GODZIK, A; PAWLOWSKI, K; REED, J C; STEHLIK, C
PATENT ASSIGNEE(S): (BURN-N) BURNHAM INST
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002026780	A2	20020404	(200250)*	EN	145
AU 2001096333	A	20020408	(200252)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002026780	A2	WO 2001-US30160	20010926
AU 2001096333	A	AU 2001-96333	20010926

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001096333	A	Based on	WO 2002026780

PRIORITY APPLN. INFO: US 2000-671760 20000926
AB WO 200226780 A UPAB: 20020807
NOVELTY - Isolated PAAD domain containing polypeptide (I) comprising 80% identity to the amino acid sequence (S1) of PAAD and nucleotide binding protein (PAN) 2-6, pyrin 2, apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC)-2 fully defined in specification, where (I) is biologically active, is new.
DETAILED DESCRIPTION - An isolated PAAD (pyrin, AIM (Absent in Melanoma), ASC (Apoptosis-associated speck-like protein containing a caspase recruitment domain) and DD (death domain)) domain containing polypeptide (I) comprising an amino acid sequence of at least 80% identity to the amino acid sequence (S1) of PAN 2-6, pyrin 2 or ASC-2, where (I) is biologically active.
INDEPENDENT CLAIMS are included for the following:
(1) an isolated PAAD domain polypeptide (II) comprising a sequence which is 80% identical to amino acid sequence (S2) of PAN 2-6, pyrin 2 or ASC-2, is biologically active;

(2) an isolated NB-ARC domain polypeptide (III) comprising amino acid sequence (S3) of 80% identity to amino acids 147-465 or 196-512 or 93-273 or 183-372 of PAN 2-6 which is biologically active;

(3) an isolated leucine-rich repeat (LRR) domain polypeptide (IV) comprises amino acid sequence (S4) of 80% identity to amino acids 620-995 or 658 or 429-1031 of PAN-2,3 and 6 which is biologically active;

(4) an isolated peptide (V) comprising at least 10 contiguous amino acids of (S1);

(5) an isolated anti-PAAD antibody (VI) having specific reactivity with (I);

(6) a cell line producing the monoclonal antibody;

(7) an isolated nucleic acid molecule (VII) encoding (I) comprises a nucleic acid encoding (S1) or that hybridizes to nucleic acid molecule encoding (S1) under high stringent conditions, where (VII) encodes a biologically active (I);

(8) an isolated nucleic acid molecule (VIII) encoding (II) comprises a nucleic acid molecule encoding (S2) or a nucleic acid molecule that hybridizes to the nucleic acid molecule encoding (S2) under high stringent conditions, where (VIII) encodes a biologically active (II);

(9) an isolated nucleic acid molecule (IX) encoding (III) comprises a nucleic acid encoding (S3) or that binds to nucleic acid encoding (S3) under high stringent condition, where (IX) encodes a biologically active (III);

(10) an isolated nucleic acid molecule (X) encoding (IV) comprises a nucleic acid molecule encoding (S4) or that binds to nucleic acid encoding (S4) under high stringent condition, where (X) encodes a biologically active (IV);

(11) an oligonucleotide (XI) comprising at least 17 nucleotides capable of specifically hybridizing with cDNA of PAN 2-6, pyrin 2 or ASC-2 or its complement;

(12) an oligonucleotide (XII) comprising at least 50 nucleotides capable of specifically hybridizing with cDNA of PAN 2-6, pyrin 2 or ASC-2 or its complement;

(13) a vector containing (VII), (VIII), (IX) or (X);

(14) a recombinant cell containing (VII), (VIII), (IX) or (X); and

(15) decreasing the expression of (I) in a cell by introducing an antisense or dsRNA molecule into a cell which binds to cDNA of PAN 2-6, pyrin 2 or ASC-2.

ACTIVITY - Cytostatic; immunosuppressive; vulnerary; **antiinflammatory**; vasotropic; antiallergic; antiulcer; dermatological; cerebroprotective; cardiant; antiparkinsonian; nootropic; neuroprotective; anti-HIV. No supporting data is given.

MECHANISM OF ACTION - Gene therapy; inhibitor of **NFkappaB** activation.

10000 293N cells were seeded into 96 well plates and cells were transfected the following using Superfect transfection reagent with 10 ng of pNFkappaB-luc Renilla luciferase (pRL-TK) reporter vectors together with 100 ng of plasmids encoding proteins in the tumor necrosis factor-alpha (TNF) pathway (pCMV, TNFR1, pcDNA3 Traf2 or pcDNA3HA RIP) and either 400 ng of pcDNA3Myc (empty) or 400 ng of pcDNA3MycPAAD1-89 (PAAD). After 36 hours, cells were harvested and activity were determined using the dual luciferase system. The cells were stimulated with 10 ng TNF- alpha for 6-8 hours prior to lysis. For empty, the TNF- alpha induction of **NFkappaB** activity was 21.05 and that of PAAD2 was 7.14. This results of **NFkappaB** activation indicated that expression of PAAD domain of PAN 2 significantly inhibited **NFkappaB** activation by TNF alpha . It was concluded that inhibition of **NFkappaB** activation by PAN 2 was mediated by the PAAD domain by expression of full length PAN 2 by transfection with pcDNA3MycPAN2 or pcNDA3MycPAAD 1-89 which was same.

USE - (XI) is useful for identifying (VII) in a sample. (VI) is

useful for detecting the presence of (I) in a sample. (I)/(II) is useful for identifying (I)-associated polypeptide (PAP). (III) or (IV) is also useful for identifying PAP. (I), (II), (III), or (IV) is useful for identifying an effective agent that alters the association of (I), (II), (II) or (IV) with PAP such as ASC, ASC2, caspase-1, card10, Nod1, NIK, **IKKi**, JKB alpha and IKAP. (I) is useful for identifying an agent that modulates PAAD domain mediated inhibition of nuclear factor kappaB (**NFkappaB**) by contacting a cell that recombinantly express (I) or inducer of **NFkappaB** with a candidate agent and detecting the **NFkappaB** activity i.e. increase or decrease in **NFkappaB** activity in cell compared to a control cell indicates that the candidate agent modulates PADD domain mediated inhibition **NFkappaB** of activity. (III) is useful for identifying an agent that modulates the activity of NB-ARC domain of (I). (VIII) is useful for modulating the transcriptional activity of **NFkappaB** in a cell (all claimed). (I) or its functional fragments is useful in altering cellular or biochemical process such as apoptosis, **NFkappaB** induction, cytokine processing, cytokine receptor signaling caspase-mediated proteolysis or c-Jun N-terminal kinase activation, thus having modulating effect on cell life and death (apoptosis) **inflammation**, cell adhesion or other cellular or biochemical processes. (I) is useful for the production of (VI). (VII) is useful for producing (I), as hybridization probe for assaying PADD domain encoding gene or mRNA transcript or as primers or templates in PCR reaction for amplifying genes encoding (I). (I) is useful for treating cancer pathologies, keratinocyte, hyperplasia, neoplasia, keloid benign prostatic hypertrophy, **inflammatory** hyperplasia, fibrosis, smooth muscle cell proliferation in arteries following balloon angioplasty (restenosis), leukemia, lymphomas; **inflammatory** diseases such as allergies, arthritis, lupus, schrojen's syndrome, Crohn's disease and ulcerative colitis, graft versus host disease, stroke, heart failure, neurodegenerative diseases such as parkinson's and Alzheimer's disease, human immuno deficiency virus infection (HIV). (I) is useful for diagnosing cancer or monitoring cancer therapy.
Dwg.0/10

L118 ANSWER 34 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-479100 [51] WPIDS
DOC. NO. NON-CPI: N2002-378362
DOC. NO. CPI: C2002-136255
TITLE: A new transgenic mouse heterozygous for a disrupted **Ikk** beta/**NEMO** gene has decreased **Ikk** beta/**NEMO** gene expression and is useful to find treatment for incontinenta pigmenti.
DERWENT CLASS: B04 D16 P14
INVENTOR(S): KARIN, M; MAKRIS, K
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002056150	A1	20020509	(200251)*		14

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002056150	A1 Provisional	US 2000-212438P	20000616
		US 2001-882507	20010615

Prepared by Toby Port 308-3534, Biotech Library

PRIORITY APPLN. INFO: US 2000-212438P 20000616; US 2001-882507 20010615

AB US2002056150 A UPAB: 20020812

NOVELTY - A transgenic nonhuman animal having a genome that comprises a transgene inserted into and disrupting the endogenous **Ikk** approx. g/**NEMO** gene resulting in decreased **Ikk** approx. g/**NEMO** expression, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a cell derived from the claimed transgenic animal;

(2) screening for biologically active agents to treat incontinentia pigmenti, comprising exposing the claimed transgenic mouse to a candidate agent and determining the effect on incontinentia pigmenti; and

(3) detecting a mutant **Ikk** approx. g/**NEMO** gene in an individual, comprising detecting **IKK** alpha and **IKK** beta expression, in the absence of **Ikk** approx. g/**NEMO** expression in biopsy material, preferably by immunoblot, Northern or Southern blot, reverse transcriptase PCR (polymerase chain reaction), single stranded conformation polymorphism analysis or conformation-sensitive gel electrophoresis.

ACTIVITY - Dermatological.

None given.

MECHANISM OF ACTION - None given.

USE - The transgenic animals are used to determine means to treat, control or prevent incontinentia pigmenti(claimed).

Dwg.0/13

L118 ANSWER 35 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-331984 [37] WPIDS

DOC. NO. CPI: C2002-095895

TITLE: Identifying inhibitor of ubiquitin mediated proteolysis of phosphorylated IkappaB, useful for inhibiting **NFkappaB** activation involves testing ability of compound to interfere with beta TrCP/E3RS-hnRNP U interaction.

DERWENT CLASS: B04 D16

INVENTOR(S): ALKALAY, I; BEN-NERIAH, Y; BEN-SHUSHAN, E; DAVIS, M; HTZUBAI, A; YARON, A; HATZUBAI, A

PATENT ASSIGNEE(S): (YISS) YISSUM RES DEV CO HEBREW UNIV JERUSALEM

COUNTRY COUNT: 97

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1182251	A1	20020227	(200237)*	EN	37
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
WO 2002016633	A2	20020228	(200237)	EN	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002022343	A	20020304	(200247)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

EP 1182251	A1	EP 2000-117429	20000811
WO 2002016633	A2	WO 2001-IB2428	20010810
AU 2002022343	A	AU 2002-22343	20010810

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002022343	A	Based on	WO 2002016633

PRIORITY APPLN. INFO: EP 2000-117429 20000811

AB EP 1182251 A UPAB: 20020613

NOVELTY - Identifying (M1) compound that modulates, in particular inhibits, ubiquitin-mediated proteolysis of phosphorylated IkappaB (inhibitor protein of **NFkappaB** activation), where the compound is tested for its capacity to directly or indirectly modulate, in particular interfere with, ability of beta -TrCP/E3RS (ubiquitin-protein ligase (E3) receptor subunit) to engage in protein-protein association involving hnRNP-U.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) use of a compound that has the capacity to interfere, directly or indirectly, with the ability of beta -TrCP/E3RS to engage in protein-protein association involving hnRNP-U for the preparation of a medicament for the treatment of disorders associated with **NF-kappaB** activation;

(2) use of a compound that inactivates the hnRNP-U protein per se, for the preparation of a medicament for the treatment of disorders associated with **NF-kappaB** activation;

(3) anti hnRNP-U antibodies for the diagnosis of condition in which the beta -TrCP/E3RS is compromised, and for monitoring the therapeutic efficacy of an inhibitor of ubiquitin-mediated proteolysis of phosphorylated IkappaB; and

(4) producing a functional beta -TrCP/E3RS, where beta -TrCP/E3RS and hnRNP-U are co-expressed, optionally together with Skp1, in a bacterial, yeast or insect cell.

ACTIVITY - Anti-HIV; immunosuppressive; antibacterial; antirheumatic; antiarthritic; antiasthmatic; cytostatic; nootropic; neuroprotective; cerebroprotective. No biodata is given in the source material.

MECHANISM OF ACTION - Modulator of **NFkappaB** activation; modulator of ubiquitin-mediated proteolysis of phosphorylated IkappaB; inhibits beta -TrCP/E3RS by inhibiting association of hnRNP-U with E3RS or by inactivating hnRNP-U.

USE - (M1) is useful for identifying a compound that modulates, in particular inhibits ubiquitin-mediated proteolysis of phosphorylated IkappaB (claimed). The beta -TrCP/E3RS inhibitors identified by the above method are useful for preparing medicaments for treating disorders associated with NFkapaB activation such as progression of acquired immunodeficiency syndrome (AIDS); activation of T-cells, B-cells and macrophages during the immune response such as acute phase response; toxic shock, transplant rejection and the response to the cell to gamma radiation and UV light. The E3RS inhibitors are useful as **antiinflammatory** drugs, and thus useful in the treatment of asthma or rheumatoid arthritis, in cancer therapy in order to increase the sensitivity of the patient to chemotherapeutic agents, in the therapy of central nervous system disorders e.g., neurodegenerative diseases such as Alzheimer's disease, stroke due to atherosclerosis; and as immunosuppressive drugs.

ADVANTAGE - The method requires fewer components than the described E3-substrate interruption assay (i.e., there is no need for any substrate, ubiquitination enzymes,) and therefore the method is simpler and accurate,

obviates the need to prepare an **IKK**-phosphorylated substrate, assay a low affinity complex which is more amenable for interruption, thus allowing the identification of a broader range of inhibitors. The method can also be applied for identifying inhibitors of cellular targets of human immunodeficiency virus (HIV), and these inhibitors are expected to be superior over the other **NFkappaB** inhibitors by inhibiting the function of both **NFkappaB** and Vpu, which are necessary for HIV replication.

DESCRIPTION OF DRAWING(S) - The figure shows Vpu-mediated CD4 degradation assay.

Dwg.7A/7

L118 ANSWER 36 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-071475 [08] WPIDS
DOC. NO. CPI: C2001-020075
TITLE: New aminoacid residue-substituted benzimidazole derivative **I(kappa)B**-kinase inhibitors, useful for treating **NF(kappa)B**-related disorders, e.g. rheumatoid arthritis, asthma, Alzheimer's disease or cancer.
DERWENT CLASS: A96 B02
INVENTOR(S): BOCK, W J; FLYNN, G A; NEISES, B; RITZELER, O; STILZ, H U; WALSER, A; HABERMANN, J; JAHNE, G; STILZ, H; JAEHNE, G
PATENT ASSIGNEE(S): (AVET) AVENTIS PHARMA DEUT GMBH
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001000610	A1	20010104	(200108)*	GE	102
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
DE 19928424	A1	20001228	(200119)		36
AU 2000054042	A	20010131	(200124)		
DE 10006297	A1	20010816	(200148)		
CZ 2001004526	A3	20020313	(200223)		
NO 2001006154	A	20020219	(200223)		
US 6358978	B1	20020319	(200224)		
BR 2000012450	A	20020402	(200231)		
EP 1194425	A1	20020410	(200232)	GE	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
SK 2001001876	A3	20020604	(200247)		
KR 2002012291	A	20020215	(200257)		
CN 1356995	A	20020703	(200265)		
HU 2002002028	B	20021028	(200277)		
JP 2003503400	W	20030128	(200309)		146
ZA 2001010127	A	20030129	(200314)		166
NZ 516348	A	20030627	(200348)		
MX 2001012283	A1	20020801	(200367)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001000610	A1	WO 2000-EP5340	20000609

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DE 19928424	A1	DE 1999-19928424	19990623
AU 2000054042	A	AU 2000-54042	20000609
DE 10006297	A1	DE 2000-10006297	20000212
CZ 2001004526	A3	WO 2000-EP5340	20000609
		CZ 2001-4526	20000609
NO 2001006154	A	WO 2000-EP5340	20000609
		NO 2001-6154	20011217
US 6358978	B1	US 2000-599390	20000622
BR 2000012450	A	BR 2000-12450	20000609
		WO 2000-EP5340	20000609
EP 1194425	A1	EP 2000-938780	20000609
		WO 2000-EP5340	20000609
SK 2001001876	A3	WO 2000-EP5340	20000609
		SK 2001-1876	20000609
KR 2002012291	A	KR 2001-716472	20011221
CN 1356995	A	CN 2000-809233	20000609
HU 2002002028	B	WO 2000-EP5340	20000609
		HU 2002-2028	20000609
JP 2003503400	W	WO 2000-EP5340	20000609
		JP 2001-507019	20000609
ZA 2001010127	A	ZA 2001-10127	20011210
NZ 516348	A	NZ 2000-516348	20000609
		WO 2000-EP5340	20000609
MX 2001012283	A1	WO 2000-EP5340	20000609
		MX 2001-12283	20011129

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000054042	A	Based on	WO 2001000610
CZ 2001004526	A3	Based on	WO 2001000610
EP 1194425	A1	Based on	WO 2001000610
SK 2001001876	A3	Based on	WO 2001000610
HU 2002002028	B	Based on	WO 2001000610
JP 2003503400	W	Based on	WO 2001000610
NZ 516348	A	Based on	WO 2001000610
MX 2001012283	A1	Based on	WO 2001000610

PRIORITY APPLN. INFO: DE 2000-10006297 20000212; DE 1999-19928424 19990623

AB WO 200100610 A UPAB: 20020411

NOVELTY - Benzimidazole derivatives (I), containing an aminoacid residue N-bonded via a carbonyl, sulfinyl or sulfonyl group, are new.

DETAILED DESCRIPTION - Benzimidazoles of formula (I) and their stereoisomers and salts are new.

At least one of R1-R4 = -D-N(R8)-CHR9-Z, any other(s) being H, halo, 1-6C alkyl, optionally substituted (os) 5-14 membered heteroaryl, os 5-12 membered heterocyclyl, CN, aryloxy, aralkoxy, alkoxy, OR11, N(R11)2, S(O)xR11, NO2 or CF3;

D = CO, SO or SO2;

R8 = H or alkyl;

R9 = characteristic residue of an aminoacid; os Q; or 1-6C alkyl (os by 1 or 2 of os Q, OR11, =O, halo, CN, CF3, S(O)xR11, COOR11, CON(R11)2, N(R11)2, 3-6C cycloalkyl, -C(R11)=C(R11)2 and -CC-R11);

or -R8-R9- = -A-X-Y-B-, the obtained ring system being os by 1-3 1-8C alkyl (os by 1 or 2 of OH, 1-8C alkoxy, halo, NO2, NH2, CF3, OH, OCH2O, COMe, CHO, CN, COOH, CONH2, alkoxycarbonyl, Ph, OPh, CH2Ph, OCH2Ph and tetrazolyl);

Z = os Q, os 1-6C alkyl or -COR10;

R10 = OR11 or N(R11)2;

R11 = H, 1-6C alkyl (os by 1-3 of os aryl, 5-14 membered heteroaryl, 5-12 membered heterocyclyl, halo, NH2, mono- or dialkylamino (where alkyl is os by 1-3 of halo and OH), 1-6C alkoxy and COOH), os aryl, 5-14 membered heteroaryl or 5-12 membered heterocyclyl;

or -R9-Z- = -T-V-W-N(R11)-C(O)-, the obtained ring system being optionally substituted as for that formed by -R8-R9-;

Q = aryl, 5-14 membered heteroaryl or 5-12 membered heterocyclyl;

A = N or CH2;

B, X, T, W = O, S, N or CH2;

Y, V = direct bond or B; or

X+Y, T+V or V+W = phenyl or 1,2-, 1,3- or 1,4-diazine residue;

R5 = H, OH or =O;

R6 = os aryl; phenyl, substituted by 1 or 2 of CN, NO2, alkoxy, N(R11)2, NHCOR11, S(O)xR11, COR11 and aminoalkyl; or 5-14 membered heteroaryl or 5-12 membered heterocyclyl, both optionally having 1-3 substituents;

provided that rings formed by R8+R9 or R9+R10 contain 0 or 1 O or S and 1-4 N; alkyl moieties have 1-4C unless specified otherwise.

An INDEPENDENT CLAIM is included for the preparation of (I).

ACTIVITY - Antirheumatic; antiarthritic; antiasthmatic; cardiant; nootropic; neuroprotective; cytostatic; antiarteriosclerotic; **antiinflammatory**; antianginal; nephrotropic; antibacterial; immunosuppressive; cerebroprotective.

MECHANISM OF ACTION - **I(kappa)B**-kinase inhibitor; **NF(kappa)B** antagonist. 3-(N-Phenyl-N-ethylamino)-2-((2-(pyrid-4-yl)-1H-benzimidazole-5-carbonylamino)-propionic acid (Ia) had an IC50 of 0.07 mu M for inhibition of **I(kappa)B**-kinase, and inhibited protein kinase A by 31% at 100 mu M.

USE - (I) are used for the treatment or prophylaxis of diseases associated with elevated **NF(kappa)B** activity, specifically rheumatoid arthritis, osteoarthritis, asthma, cardiac infarction, Alzheimer's disease, cancer or atherosclerosis (all claimed). Other disclosed to be treated are **inflammation**, cardiac insufficiency, acute coronary syndrome, septic shock, unstable angina pectoris, acute and chronic renal failure and stroke.

ADVANTAGE - (I) are potent and highly specific inhibitors of **I(kappa)B** kinase (involved in the first stage of the signal cascade for activation of **NF(kappa)B**).

Dwg.0/0

L118 ANSWER 37 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-443102 [48] WPIDS
DOC. NO. CPI: C2001-134157
TITLE: New carbamoyl or sulfamoyl-substituted indole derivatives, are **NF(kappa)B** antagonists and **I(kappa)B** kinase inhibitors useful e.g. for treating rheumatoid arthritis, asthma, Alzheimer's disease or cancer.
DERWENT CLASS: A96 B02
INVENTOR(S): HABERMANN, J; JAEHNE, G; NEISES, B; RITZELER, O; STILZ, H U; FITZELER, O; STILZ, H
PATENT ASSIGNEE(S): (AVET) AVENTIS PHARMA DEUT GMBH
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 19951360	A1	20010503	(200148)*		20
WO 2001030774	A1	20010503	(200148)	GE	

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001012728 A 20010508 (200149)
NO 2002001808 A 20020417 (200247)
BR 2000015026 A 20020716 (200255)
CZ 2002001413 A3 20020717 (200260)
EP 1261601 A1 20021204 (200280) GE
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
SK 2002000543 A3 20021106 (200281)
ZA 2002003204 A 20030129 (200314) 56
CN 1379772 A 20021113 (200317)
HU 2002003228 A2 20030228 (200330)
KR 2003004302 A 20030114 (200333)
US 2003119820 A1 20030626 (200343)
JP 2003519101 W 20030617 (200349) 76

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
DE 19951360	A1		DE 1999-19951360	19991026
WO 2001030774	A1		WO 2000-EP10210	20001017
AU 2001012728	A		AU 2001-12728	20001017
NO 2002001808	A		WO 2000-EP10210	20001017
			NO 2002-1808	20020417
BR 2000015026	A		BR 2000-15026	20001017
			WO 2000-EP10210	20001017
CZ 2002001413	A3		WO 2000-EP10210	20001017
			CZ 2002-1413	20001017
EP 1261601	A1		EP 2000-974405	20001017
			WO 2000-EP10210	20001017
SK 2002000543	A3		WO 2000-EP10210	20001017
			SK 2002-543	20001017
ZA 2002003204	A		ZA 2002-3204	20020423
CN 1379772	A		CN 2000-814472	20001017
HU 2002003228	A2		WO 2000-EP10210	20001017
			HU 2002-3228	20001017
KR 2003004302	A		KR 2002-705395	20020426
US 2003119820	A1	Cont of	US 2000-695412	20001025
			US 2002-263691	20021004
JP 2003519101	W		WO 2000-EP10210	20001017
			JP 2001-533128	20001017

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001012728	A	Based on	WO 2001030774
BR 2000015026	A	Based on	WO 2001030774
CZ 2002001413	A3	Based on	WO 2001030774
EP 1261601	A1	Based on	WO 2001030774
SK 2002000543	A3	Based on	WO 2001030774
HU 2002003228	A2	Based on	WO 2001030774
JP 2003519101	W	Based on	WO 2001030774

PRIORITY APPLN. INFO: DE 1999-19951360 19991026
AB DE 19951360 A UPAB: 20010829

NOVELTY - Carbamoyl or sulfamoyl-substituted indole derivatives (I) are new.

DETAILED DESCRIPTION - Indole derivatives of formula (I) and their stereoisomers and/or salts are new.

one of R1-R4 = -D-N(R7)-CHR8-Z' or N-heterocyclic-containing group of formula (i) or (i), where the ring in (i) is optionally substituted by 1-8C alkyl or by 1-2 Q groups and the ring in (ii) is optionally substituted by 1-3 Q groups;

the remainder of R1-R4 = H, halo, optionally substituted aryl, optionally substituted 5-14 membered heteroaryl, optionally substituted 5-12 membered heterocyclyl or 1-6C alkyl; and

up to 2 of the remainder R1-R4 = H, CN, OR10, N(R10)2, CF3;S(O)xR10, halo or

x = 0-2;

R5 = H, OH or =O;

R6 = aryl, 5-14 membered heteroaryl or 5-12 membered heterocyclyl all optionally substituted;

D = C(O), SO or SO2;

R7 = H or 1-4C alkyl;

R8 = R9 or the characteristic residue of an amino acid;

R9 = aryl optionally substituted, 5-14 membered heteroaryl optionally substituted, 5-12 membered heterocyclyl optionally substituted or 1-5C alkyl (optionally substituted by 1-3 of optionally substituted aryl, optionally substituted 5-14 membered heteroaryl, optionally substituted 5-12 membered heterocyclyl, OR10, =O, halo, CN, CF3, S(O)xR10, COOR10, CON(R10)2, N(R10)2, 3-6C cycloalkyl, -C(R10)=C(R10)2 or -CC-R10; halo or CF3;

R10 = H, 1-6C alkyl (optionally substituted by aryl, 5-14 membered heteroaryl, 5-12 membered heterocyclyl, halo, '-N-(1-6C)n-alkyl' (sic) (where n = 0-2 and alkyl is optionally substituted by 1-3 of halo or COOH) or COOH), optionally substituted aryl, optionally substituted 5-14 membered heteroaryl or optionally substituted 5-12 membered heterocyclyl;

Z' = optionally substituted aryl, optionally substituted 5-14 membered heteroaryl, optionally substituted 5-12 membered heterocyclyl or COR11;

R11 = OR10 or N(R10)2;

A = N or CH2;

B', X, T, W = O, S, N or CH2;

Y, V = direct bond or as for B';

or X-Y, T-V or V-W = phenyl or 1,2-, 1,3- or 1,4-diazine residue;

Q = OH, 1-8C alkoxy, halo, NO2, NH2, OH, OCH2O, COMe, CHO, CN, COOH, CONH2, (1-4C) alkoxycarbonyl, Ph, OPh, benzyl, benzyloxy or tetrazolyl; and

Ph = phenyl.

With the proviso that the ring in (i) or (ii) contains not more than one of O and S and contains 1-4 N; and X is not O, S or N if A = N.

An INDEPENDENT CLAIM is included for the preparation of (I).

ACTIVITY - Antirheumatic; antiarthritic; antiasthmatic; cardiant; neuroprotective; nootropic; cytostatic; antiarteriosclerotic; **antiinflammatory**.

MECHANISM OF ACTION - **NF(kappa)B** antagonist; **I(kappa)B**-kinase inhibitor.

2-Pyridin-4-yl-1H-indole-5-carboxylic acid (1-carbamoyl-2-phenylsulfanyl-ethyl)-amide (Ia) had IC50 0.55 micro M for inhibition of **I(kappa)B**-kinase; and at 100 micro M inhibited protein kinase A.by 35%, protein kinase C by 39% and casein kinase II by 37%.

USE - (I) are used for the treatment or prophylaxis of diseases associated with elevated **NF(kappa)B** activity, specifically rheumatoid arthritis, osteoarthritis, asthma, cardiac infarction, Alzheimer's disease, cancer diseases or atherosclerosis (all

claimed). The action against rheumatoid arthritis is based on **antiinflammatory** activity; and the action against cancer diseases is based on potentiation of cytotoxic therapy.
ADVANTAGE - (I) are potent and highly specific inhibitors of **I(kappa)B** kinase.
Dwg.0/0

L118 ANSWER 38 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-350748 [30] WPIDS
DOC. NO. CPI: C2000-106774
TITLE: Novel **I-kappa-B** kinase, **IKK**-i, capable of activating transcription factor **NF-kappa-B** to inhibit expression of gene relating to immune response, useful in drug compositions to treat **inflammation** and improve immune response mechanism.
DERWENT CLASS: B04 D16
INVENTOR(S): AKIRA, S; SHIMADA, T
PATENT ASSIGNEE(S): (NISC-N) JAPAN SCI & TECHNOLOGY CORP
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000024908	A1	20000504	(200030)*	JA	52
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: CA JP US					
EP 1043397	A1	20001011	(200052)	EN	
R: AL DE FR GB LT LV MK RO SI					
JP 2000578460 X		20020129	(200212)		
US 2003059419 A1		20030327	(200325)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000024908	A1		WO 1999-JP5916	19991026
EP 1043397	A1		EP 1999-949429	19991026
			WO 1999-JP5916	19991026
JP 2000578460	X		WO 1999-JP5916	19991026
			JP 2000-578460	19991026
US 2003059419	A1	Div ex	WO 1999-JP5916	19991026
		Div ex	US 2000-582397	20000623
			US 2002-298402	20021118

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1043397	A1	Based on	WO 2000024908
JP 2000578460	X	Based on	WO 2000024908

PRIORITY APPLN. INFO: JP 1998-304085 19981026
AB WO 200024908 A UPAB: 20000624
NOVELTY - A protein which can activate transcriptional factor **NF-kappa-B**, having a 716 (human) or 717 (mouse) residue amino acid sequence, fully defined in the specification, or a sequence based on them, but with deletions, substitutions and/or additions, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a gene with a base sequence that encodes the novel protein; and

(2) a drug composition containing the protein and a carrier.
ACTIVITY - **Antiinflammatory**; immunestimulant.
MECHANISM OF ACTION - Serine/threonine kinase; **I-kappa-B** kinase (**IKK**-i).
USE - The protein is useful in drug compositions to treat **inflammation** and improve immune response mechanism, and also applicable in preventing and treating diseases associated with the I-TRAF or TRAF molecule (claimed).
Dwg.0/15

L118 ANSWER 39 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-610247 [52] WPIDS
DOC. NO. CPI: C1999-177635
TITLE: Isolated nucleic acids encoding a **I-kappa-B** kinase binding protein designated Y2H61, useful for studying and modulating the function of **I-kappa-B** kinase and its role in cell division, **inflammation** and apoptosis.
DERWENT CLASS: B04 D16
INVENTOR(S): MARCU, K B
PATENT ASSIGNEE(S): (UYNY) UNIV NEW YORK STATE RES FOUND
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5972655	A	19991026	(199952)*		8

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5972655	A	US 1998-196048	19981119

PRIORITY APPLN. INFO: US 1998-196048 19981119
AB US 5972655 A UPAB: 19991210
NOVELTY - Isolated nucleic acids (I) encoding **I-kappa-B** kinase (**IKK**) binding proteins (designated Y2H61), which have a defined amino acid sequence given in the specification (or allelic variants of it), are new.
DETAILED DESCRIPTION - Isolated nucleic acids encoding **I-kappa-B** kinase (**IKK**) binding proteins, which have a defined sequence given in the specification (or allelic variants of it), are new. **I-kappa-B** proteins are inhibitory proteins which anchor **NF-kappa-B** transcription factors (TFs). **NF-kappa-B** TFs mediate the expression of proteins involved in cell division, **inflammation** and apoptosis in response to extracellular signal factors. If the **NF-kappa-B** TF is to be released and become active, the **I-kappa-B** protein which anchors and inhibits it must be phosphorylated. This phosphorylation is catalyzed by **IKK** proteins. Therefore **IKK** activity is essential for cell division, **inflammation** and apoptosis. The **IKK** binding protein Y2H61 binds to **IKK** and modulates its activity.
INDEPENDENT CLAIMS are also included for the following:
(i) an isolated nucleic acid (I') fully complementary to (I); and
(ii) a method of making **IKK** binding proteins, comprising:
(1) transforming a host cell with (I);
(2) expressing the nucleic acid molecules; and

(3) isolating the **IKK** binding protein.

ACTIVITY - **Anti-inflammatory**; anti-apoptotic; anti-proliferative.

MECHANISM OF ACTION - The **IKK** binding protein binds to **IKK**.

A yeast two hybrid screen was undertaken with **IKK** alpha as a bait in an attempt to identify interacting proteins which could represent in vivo regulators of the cytokine induced kinase cascade. Full length **IKK** alpha and smaller fragments in the Field's pGTB9c bait vector (see Fields et al., Trends Genet., (1994)) met with technical problems owing to its inherent in vivo transactivation properties. These problems were overcome by incorporating a high dose of an inhibitor of the product of the His3 selection gene therefore severely restricting yeast colony growth. (Triazole or 3-AT (3-amino-1,2,4-triazole or aminotriazole) had been reported to competitively inhibit the product of the yeast His3 gene in a dose dependent manner (see Klopotowski et al., Arch. Biochem. Biophys., (1965)). The bait vector's insert was a 937 base pair SnaB1/XhoI fragment of the murine **IKK** alpha clone encoding the protein's leucine zipper, helix-loop-helix and carboxyl terminus. The latter bait vector was transfected into the Y153 yeast strain and a colony that grew on agar without tryptophan was selected for further transfections according to standard protocols (see Yeast Matchmaker Manual, Clontech Inc.). Yeast harboring the bait grew on histidine-minus plates. However, this nonspecific growth was abrogated by the inclusion of 50 mu M (3-AT) that would also yield the strongest interactors. Y153 cells harboring the bait vector were transfected with a B lymphoblast cDNA library (0.6 x 109 colony forming units ATCC 87003) (see Durfee et al., Genes Dev., (1993)) sub-cloned into plasmid BNN132 (for a final transfection frequency of 105 clones), which were spread onto 30 agar plates (His-, Trp-, Leu-, 50 mM 3-AT). 126 clones showing a faster growth rate compared to background colonies were picked after 3 and 6 days incubation at 30 deg. C and replated. 70 clones were selected for plasmid isolation based on their growth on His-, Trp-, Leu-, 50 mu M 3-AT plates. From these 70, 16 clones remained positive after multiple rounds of purification and rescreening (14 of these sixteen were unique and two were isolated twice).

These results demonstrate the presence of a family of **IKK** alpha binding proteins. 9 of the 14 clones were known proteins and the remaining five specified novel proteins (3 of which interacted with the bait more strongly than **IKK** alpha 's **I-kappa -B** beta substrate (Y2h35, 53 and 56), one in a comparable fashion to **I-kappa-B** beta (Y2h14) and one exhibited weaker binding (Y2H61). Several of the known proteins were involved in either signaling and/or molecular trafficking pathways in cells.

USE - (I) may be used in the recombinant production of **IKK** binding proteins. These may then be used to study and modulate the function of **IKK** and its role in cell division, **inflammation** and apoptosis.

Dwg.0/0

L118 ANSWER 40 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-467580 [40] WPIDS
DOC. NO. CPI: C1998-141851
TITLE: Nucleic acid encoding **I-kappa-B** kinase subunits and antibodies - the subunits phosphorylate the inhibitor of **NF-kappa -B**, for studying the **inflammatory** response and signal transduction pathways.
DERWENT CLASS: B04 D16
INVENTOR(S): DIDONATO, J A; HAYAKAWA, M; KARIN, M; ROTHWARF, D M; ZANDI, E

PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA; (DIDO-I) DIDONATO J A; (HAYA-I) HAYAKAWA M; (KARI-I) KARIN M; (ROTH-I) ROTHWARF D M; (ZAND-I) ZANDI E
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9837228	A1	19980827	(199840)*	EN	100
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP					
AU 9866646	A	19980909	(199905)		
EP 981642	A1	20000301	(200016)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6242253	B1	20010605	(200133)		
US 6268194	B1	20010731	(200146)		
AU 740622	B	20011108	(200176)		
JP 2001524813	W	20011204	(200203)		83
US 2002045235	A1	20020418	(200228)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9837228	A1		WO 1998-US3511	19980223
AU 9866646	A		AU 1998-66646	19980223
EP 981642	A1		EP 1998-908673	19980223
			WO 1998-US3511	19980223
US 6242253	B1	Provisional	US 1997-61470P	19971009
			US 1998-168629	19981008
US 6268194	B1		US 1997-810131	19970225
AU 740622	B		AU 1998-66646	19980223
JP 2001524813	W		JP 1998-536953	19980223
			WO 1998-US3511	19980223
US 2002045235	A1	Provisional	US 1997-61470P	19971009
		Div ex	US 1998-168629	19981008
			US 2001-796872	20010228

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9866646	A	Based on	WO 9837228
EP 981642	A1	Based on	WO 9837228
AU 740622	B	Previous Publ.	AU 9866646
		Based on	WO 9837228
JP 2001524813	W	Based on	WO 9837228
US 2002045235	A1	Div ex	US 6242253

PRIORITY APPLN. INFO: US 1997-61470P 19971009; US 1997-810131 19970225; US 1998-168629 19981008; US 2001-796872 20010228

AB WO 9837228 A UPAB: 19981008
An isolated nucleic acid molecule (I) is new, comprising a nucleotide sequence (NS) encoding an **I-kappa B** kinase (**IKK**) subunit, **IKK** beta , which phosphorylates the inhibitor of **NF-kappa**-B (IkB alpha) on serine-32 and serine-36, and has a molecular mass of about 87 kD, or a nucleotide complementary to this, or a portion.

Also new are: (a) an isolated nucleic acid molecule comprising a NS encoding a full length human **IKK**, **IKK** alpha , which

phosphorylates as above and has a molecular mass of about 85 kD, or a complementary NS; (b) a vector containing (I) or (a); (c) a host cell containing (b); (d) a peptide of at least 3 contiguous amino acids (AAs) encoded by (I); (e) isolated human **IKK** beta and **IKK** alpha subunits defined as above, or a portion; (f) an antibody specifically binding an epitope of a peptide above; and (g) a cell line producing (f).

USE - The nucleic acids, subunits and antibodies may be used to study the signal transduction pathways involved in the **inflammatory** and immune responses. The **IKK** subunits may be used to identify agents that regulate the specific association of an **IKK** subunit and a second protein, in vitro or in vivo in a cell culture (mammalian or yeast). The subunits may also be used to identify agents that alter **IKK** activity, such as protein kinase inhibitors. The antibodies are used to isolate **IKK** from samples, preferably antibodies that bind to the alpha and beta subunits or to tags linked to the subunits, e.g. a peptide tag such as haemagglutinin, HIS6 and FLAG.

Dwg.0/3

L118 ANSWER 41 OF 41 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-179440 [16] WPIDS
DOC. NO. NON-CPI: N1998-141901
DOC. NO. CPI: C1998-057741
TITLE: New isolated stimulus-inducible **I-kappa -B** kinase signalsome - useful for developing products for treating, e.g. **inflammatory** neuro-degenerative and auto-immune diseases.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BARBOSA, M; LI, G; MERCURIO, F; MURRAY, B W; ZHU, H; LI, J W
PATENT ASSIGNEE(S): (SIGN-N) SIGNAL PHARM INC; (BARB-I) BARBOSA M; (LIJW-I) LI J W; (MERC-I) MERCURIO F; (MURR-I) MURRAY B W; (ZHUH-I) ZHU H
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9808955	A1	19980305	(199816)*	EN	115
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP					
AU 9740904	A	19980319	(199831)		
EP 920518	A1	19990609	(199927)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 5972674	A	19991026	(199952)		
AU 726383	B	20001102	(200062)		
JP 2001502892	W	20010306	(200116)		106
US 6258579	B1	20010710	(200141)		
US 2002151021	A1	20021017	(200270)		
US 2003100026	A1	20030529	(200337)		
US 6576437	B2	20030610	(200340)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9808955	A1	WO 1997-US15003	19970826
AU 9740904	A	AU 1997-40904	19970826
EP 920518	A1	EP 1997-938616	19970826
		WO 1997-US15003	19970826
US 5972674	A	US 1996-697393	19960826

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AU 726383	B		AU 1997-40904	19970826
JP 2001502892	W		WO 1997-US15003	19970826
			JP 1998-511840	19970826
US 6258579	B1	CIP of	US 1996-697393	19960826
			US 1997-910820	19970813
US 2002151021	A1	CIP of	US 1996-697393	19960826
		Div ex	US 1997-910820	19970813
			US 2001-844908	20010427
US 2003100026	A1	CIP of	US 1996-697393	19960826
		Div ex	US 1997-910820	19970813
		Div ex	US 2001-844908	20010427
			US 2003-338462	20030108
US 6576437	B2	CIP of	US 1996-697393	19960826
		Div ex	US 1997-910820	19970813
			US 2001-844908	20010427

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9740904	A	Based on	WO 9808955
EP 920518	A1	Based on	WO 9808955
AU 726383	B	Previous Publ.	AU 9740904
		Based on	WO 9808955
JP 2001502892	W	Based on	WO 9808955
US 6258579	B1	CIP of	US 5972674
US 2003100026	A1	CIP of	US 5972674
		Div ex	US 6258579
US 6576437	B2	CIP of	US 5972674
		Div ex	US 6258579

PRIORITY APPLN. INFO: US 1997-910820 19970813; US 1996-697393 19960826; US 2001-844908 20010427; US 2003-338462 20030108

AB WO 9808955 A UPAB: 19980421

The following are claimed: (1) a stimulus-inducible IkappaB kinase (**IKK**) 'signalsome' capable of specifically phosphorylating IkappaB alpha at residues S32 and S36, and IkappaB beta at residues 19 and 23, without the addition of exogenous cofactors; (2) a polypeptide comprising a component of an **IKK** signalsome as in (1), or its variant having a 756 aa sequence (I) (given in the specification); (3) an isolated DNA molecule encoding a polypeptide of (2); (4) a recombinant expression vector comprising a DNA of (3); (5) a host cell transformed with an expression vector of (4); (6) a method for phosphorylating a substrate of an **IKK** signalsome, comprising contacting a substrate with a polypeptide comprising a component of an **IKK** signalsome having an **IKK** activity, to phosphorylate the substrate; (7) a therapeutic composition comprising an agent that modulates **IKK** signalsome activity with a carrier, for modulating a nuclear factor (**NF**)-**kappaB** activity in a patient; (8) an antibody binding to **IKK**-1 having a 745 aa sequence (II) (given in the specification) and/or **IKK**-2 having a sequence as in (I); (9) a method for identifying an upstream kinase in the **NF-kappaB** signal transduction cascade, comprising evaluating the ability of a candidate upstream kinase to phosphorylate and induce enzymatic activity of an **IKK** signalsome or its component or variant, to identify an upstream kinase in the transduction cascade, and (10) a method for identifying a component of an **IKK** signalsome, comprising: (a) isolating an **IKK** signalsome; (b) separating the signalsome into components, and (c) obtaining a partial sequence of a component, and thereby identifying a component of an **IKK**

signalsome.

USE - The products can be used to identify agents (claimed) that inhibit or stimulate signal transduction via the **NF-kappaB** cascade. The therapeutic composition comprising an agent may be used for treating a patient afflicted with a disorder associated with the activation of an **IKK** signalsome (claimed). The agents may be used to treat, e.g. **inflammatory**, neurodegenerative diseases and autoimmune diseases, cancer and viral infections. The antibodies may be used in a kit for detecting **IKK** signalsome activity in a sample (claimed).

Dwg.0/15

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